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XUM

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Kinetics of the bromination of *m*-nitrophenol in aqueous solution. By R. P. BELL and T. SPENCER

o-Acetylbenzamide. By A. H. REES

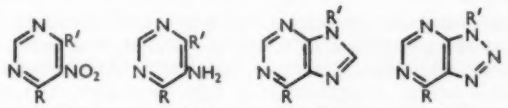
XUM

99. *The Synthesis of Some 9-Furfurylpurines and Some Related Heterocyclic Compounds.*

By R. HULL.

The synthesis is described of some 9-furfurylpurines and related triazolopyrimidines from the appropriate 5-amino-4-furfurylaminopyrimidines.

A PREVIOUS paper [1] described the preparation of 6-amino-9-furfurylpurine as a possible antiviral agent which might antagonise the formation of nucleic acid. This work has now been extended to other derivatives of 9-furfurylpurine. Corresponding 8-azapurines (*v*-triazolo[*d*]pyrimidines) were also synthesised because of the many features of biological interest found in "aza"-analogues of naturally occurring metabolites.[2] During the completion of this work Timmis, Cooke, and Spickett [3] have independently described the synthesis of some related 9-substituted purines.



(I) (II) (III) (IV)

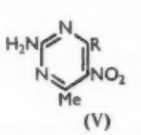
Synthesis of 6-dimethylamino-9-furfurylpurine (III; R = NMe_2, R′ = C_5H_5O) and its analogue (IV; R = NMe_2, R′ = C_5H_5O) involved the intermediates (I and II; R = NMe_2, R′ = $NH{\cdot}C_5H_5O$). Analogous intermediates were used for the furfuryl- (III; R = R′ = C_5H_5O) and morpholino-purine (III; R = morpholino, R′ = C_5H_5O) and their analogues (IV; R = R′ = C_5H_5O; and R = morpholino, R′ = C_5H_5O).

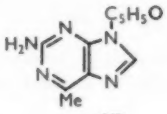
4 : 6-Dichloro-5-nitropyrimidine (I; R = R′ = Cl), the key intermediate, was obtained by the action of phosphoryl chloride and dimethylaniline on **4 : 6-dihydroxy-5-nitropyrimidine**.[4] During the preparation of large quantities, 4-chloro-6-methylanilino-5-nitropyrimidine (I; R = Cl, R′ = NMePh) was isolated as a by-product: a similar side reaction has been noticed in other chlorinations.[5] Replacement of one of the halogens can be accomplished by ammonia [4] or by mono- [6] or di-methylamine acetate.[7] However, yields may be so low as to limit this procedure.[8] In our experiments, 2 mols. of morpholine reacted with one of **4 : 6-dichloro-5-nitropyrimidine** and gave the monosubstituted pyrimidine (I; R = Cl, R′ = morpholino) in reasonable yield. Under similar conditions, however, 2 mols. of furfurylamine and triethylamine gave the disubstituted pyrimidine (I; R = R′ = $NH{\cdot}C_5H_5O$). 4-Chloro-6-furfurylamino-5-nitropyrimidine (I; R = Cl, R′ = $NH{\cdot}C_5H_5O$) was obtained upon treating the dichloro-compound (I; R = R′ = Cl) with stoicheiometric proportions of triethylamine and furfurylamine acetate.

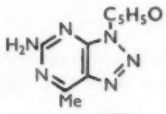
Replacement of the second chlorine atom in compounds (I; R = Cl, R′ = NMe_2 and morpholino) by furfurylamine and subsequent reduction with Raney nickel at laboratory temperature gave the aminopyrimidines (II; R = NMe_2 and morpholino, R′ = $NH{\cdot}C_5H_5O$). Cyclisation of the 5-aminopyrimidines, including (II; R = R′ = $NH{\cdot}C_5H_5O$), then led,

[1] Hull, *J.*, 1958, 2746.
[2] Barlow and Welch, *J. Amer. Chem. Soc.*, 1956, **78**, 1258.
[3] Timmis, Cooke, and Spickett, "Ciba Foundation Symposium on the Chemistry and Biology of Purines," Churchill Ltd., London 1957, p. 134.
[4] Boon, Jones, and Ramage, *J.*, 1951, 96.
[5] King, King, and Spensley, *J.*, 1947, 1247; Ross, *J.*, 1948, 1129.
[6] Brown, *J. Appl. Chem.*, 1957, **7**, 109; Robins and Lin, *J. Amer. Chem. Soc.*, 1957, **79**, 492.
[7] Rose, *J.*, 1954, 4116.
[8] Boon, *J.*, 1957 2146.

either to the purines (III; R = NMe_2 and morpholino, R′ = C_5H_5O) and (III; R = $NH{\cdot}C_5H_5O$, R′ = C_5H_5O) with acetic anhydride and ethyl orthoformate, or to the triazolopyrimidines (IV; R = NMe_2, and morpholino, R′ = C_5H_5O) and (IV; R = $NH{\cdot}C_5H_5O$, R′ = C_5H_5O) by treatment with nitrous acid.


(V)


(VI)


(VII)

A similar series of reactions was carried out with the chloropyrimidine (V; R = Cl), obtained from the readily accessible hydroxypyrimidine (V; R = OH), which yielded the purine (VI) and the triazolopyrimidine (VII), the last compound having been reported by Timmis *et al.*[3]

Experimental

4-Chloro-6-methylanilino-5-nitropyrimidine.—4 : 6-Dichloro-5-nitropyrimidine was prepared from 4 : 6-dihydroxy-5-nitropyrimidine according to the method of Boon, Jones, and Ramage,[4] and recrystallised from light petroleum (b. p. 80—100°). After storage the mother-liquors deposited yellow plates which crystallised from light petroleum, to give 4-chloro-6-methylanilino-5-nitropyrimidine, m. p. 128—130° (Found: C, 50·4; H, 3·4; N, 21·6; Cl, 13·5. $C_{11}H_9O_2N_4Cl$ requires C, 49·9; H, 3·4; N, 21·2; Cl, 13·4%).

4-Dimethylamino-6-furfurylamino-5-nitropyrimidine.—4-Chloro-6-dimethylamino-5-nitropyrimidine[7] (6 g.) in dioxan (50 ml.) was added to a stirred solution of furfurylamine (5·5 g.) in dioxan (15 ml.) at 15—20°. After 1½ hr., water (250 ml.) was added and the *product* (6 g.; m. p. 80°) collected. It crystallised from alcohol in yellow needles, m. p. 85—86° (Found: C, 50·2; H, 4·8; N, 27·0. $C_{11}H_{13}O_3N_5$ requires C, 50·2; H, 4·9; N, 26·6%).

5-Amino-4-dimethylamino-6-furfurylaminopyrimidine.—4-Dimethylamino-6-furfurylamino-5-nitropyrimidine (3·3 g.) in methanol (35 ml.), hydrogenated over Raney nickel at room temperature and pressure and worked up in the usual manner, gave the *aminopyrimidine* which crystallised from aqueous alcohol as plates (2·7 g.; m. p. 145°) (Found: C, 56·7; H, 6·3; N, 30·7. $C_{11}H_{15}ON_5$ requires C, 56·65; H, 6·4; N, 30·05%).

6-Dimethylamino-9-furfurylpurine.—5-Amino-4-dimethylamino-6-furfurylaminopyrimidine (1·17 g.) in ethyl orthoformate (7 ml.) and acetic anhydride (7 ml.) was heated under reflux during 1½ hr. Excess of reagent was removed under diminished pressure, and water was added to the residue. The *product* (0·85 g.) crystallised from aqueous alcohol in needles, m. p. 117—118° (Found: C, 59·3; H, 5·4; N, 29·0. $C_{12}H_{13}ON_5$ requires C, 59·3; H, 5·35; N, 28·8%).

6-Dimethylamino-1′-furfuryl-1′ : 2′ : 3′-triazolo(5′ : 4′-4 : 5)pyrimidine.—Sodium nitrite (0·25 g.) in water (3 ml.) was added to a solution of 5-amino-4-dimethylamino-6-furfurylaminopyrimidine (0·8 g.) in acetic acid (10 ml.) at 10°. After ½ hr. the solution was added to water (70 ml.) and the *triazolopyrimidine* (0·85 g.) was collected and washed with water. It crystallised from aqueous alcohol in pale yellow needles, m. p. 116° (Found: C, 53·6; H, 5·3; N, 33·7. $C_{11}H_{12}ON_6$ requires C, 54·1; H, 4·9; N, 34·3%).

4-Chloro-6-morpholino-5-nitropyrimidine.—Morpholine (5·3 g.) in methanol (20 ml.) was added slowly to a stirred solution of 4 : 6-dichloro-5-nitropyrimidine (5·8 g.) in methanol (100 ml.) at 4° ± 2°. After 2 hr. the solid (5·6 g.) was collected and washed with water. Recrystallisation from light petroleum (b. p. 80—100°) gave the *morpholinopyrimidine* as yellow needles, m. p. 101—102° (Found: C, 39·9; H, 4·0; N, 23·3. $C_8H_9O_3N_4Cl$ requires C, 39·25; H, 3·7; N, 22·9%).

4-Furfurylamino-6-morpholino-5-nitropyrimidine.—Furfurylamine (0·5 g.) and triethylamine (0·5 g.) in dioxan (5 ml.) were added slowly to a stirred solution of 4-chloro-6-morpholino-5-nitropyrimidine (1·2 g.) in dioxan (10 ml.) at 15—20°. After a further ½ hr. excess of water was added and the *product* (1·5 g.; m. p. 134—135°) collected. It crystallised from alcohol in pale yellow needles, m. p. 140—141° (Found: C, 51·4; H, 5·1; N, 23·6. $C_{13}H_{15}O_4N_5$ requires C, 51·2; H, 4·9; N, 23·0%).

5-Amino-4-furfurylamino-6-morpholinopyrimidine.—4-Furfurylamino-6-morpholino-5-nitropyrimidine (3·05 g.) in methanol (100 ml.), hydrogenated over Raney nickel at room temperature and pressure and worked up in the usual manner, gave the *aminopyrimidine* (2·8 g.). It crystallised from water in needles, m. p. 145° (Found: C, 56·5; H, 6·3; N, 25·1. $C_{13}H_{17}O_2N_5$ requires C, 56·7; H, 6·2; N, 25·45%).

9-Furfuryl-6-morpholinopurine.—5-Amino-4-furfurylamino-6-morpholinopyrimidine (2·75 g.) in ethyl orthoformate (12 ml.) and acetic anhydride (12 ml.) was heated under reflux during 1 hr. Excess of reagent was removed under diminished pressure and the residue was treated with 2·5N-sodium hydroxide (15 ml.) and alcohol (20 ml.) at 30—40° during 15 min. Excess of alcohol was removed under diminished pressure. The *product* (2·4 g.; m. p. 85°) crystallised from light petroleum (b. p. 100—120°) in prismatic needles, m. p. 88—89° (Found: C, 58·8; H, 5·5; N, 24·5. $C_{14}H_{15}O_2N_5$ requires C, 58·95; H, 5·2; N, 24·55%).

1′-Furfuryl-6-morpholino-1′ : 2′ : 3′-triazolo(5′ : 4′-4 : 5)pyrimidine.—Sodium nitrite (0·14 g.) in water (1·5 ml.) was added to a solution of 5-amino-4-furfurylamino-6-morpholinopyrimidine (0·5 g.) in acetic acid (4 ml.) at 10°. After 1½ hr. the solution was diluted with water and the *triazolopyrimidine* (0·5 g.) collected. It crystallised from alcohol in needles, m. p. 130—131° (Found: C, 55·0; H, 5·0; N, 29·0. $C_{13}H_{14}O_2N_6$ requires C, 54·55; H, 4·9; N, 29·35%).

4 : 6-Bisfurfurylamino-5-nitropyrimidine.—4 : 6-Dichloro-5-nitropyrimidine (55 g.) in methanol (500 ml.) was added in ½ hr. to a stirred solution of furfurylamine (55 g.) and triethylamine (57·5 g.) in methanol (200 ml.) at 15—20°. After a further 1 hr. the *product* (77 g.) was collected and washed with water. It crystallised from aqueous alcohol as pale brown needles, m. p. 131° (Found: C, 53·3; H, 4·5; N, 21·8. $C_{14}H_{13}O_4N_5$ requires C, 53·3; H, 4·1; N, 22·2%).

5-Amino-4 : 6-bisfurfurylaminopyrimidine.—4 : 6-Bisfurfurylamino-5-nitropyrimidine (16·5 g.) in methanol was hydrogenated over Raney nickel at room temperature and pressure and worked up in the usual manner. It gave the *aminopyrimidine* (14·8 g.) as plates, m. p. 114—116°, from light petroleum (b. p. 100—120°) (Found: C, 59·4; H, 5·9; N, 25·4. $C_{14}H_{15}O_2N_5$ requires C, 59·0; H, 5·3; N, 24·6%).

9-Furfuryl-6-furfurylaminopurine.—5-Amino-4 : 6-bisfurfurylaminopyrimidine (1·0 g.) in ethyl orthoformate (5 ml.) and acetic anhydride (5 ml.) was heated under reflux during 1 hr. Excess of reagent was removed under diminished pressure and the residue was then treated with 2·5N-sodium hydroxide (10 ml.) and alcohol (5 ml.) at 40° during 15 min. After cooling, the solid (1·05 g.) was collected and washed with water. Recrystallisation from water gave the *purine* as needles, m. p. 140° (Found: C, 60·4; H, 4·6; N, 23·0. $C_{15}H_{13}O_2N_5,\frac{1}{3}H_2O$ requires C, 59·8; H, 4·55; N, 23·25%).

1′-Furfuryl-6-furfurylamino-1′ : 2′ : 3′-triazolo(5′ : 4′-4 : 5)pyrimidine.—Sodium nitrite (0·73 g.) in water (3·5 ml.) was added slowly to a solution of 5-amino-4 : 6-bisfurfurylaminopyrimidine (2·85 g.) in acetic acid (40 ml.) at 15—20°. After ½ hr., the solution was added to water (250 ml.), and the *triazolopyrimidine* (2·4 g.) collected and washed with water. It crystallised from aqueous alcohol in needles, m. p. 124—126° (Found: C, 57·3; H, 4·0; N, 29·0. $C_{14}H_{12}O_2N_6$ requires C, 56·8; H, 4·05; N, 28·4%).

2-Amino-4-furfurylamino-6-methyl-5-nitropyrimidine.—Furfurylamine (4·0 g.) was added to a hot filtered solution of 2-amino-4-chloro-6-methyl-5-nitropyrimidine [4] (3·5 g.) in alcohol (80 ml.), and the whole was heated under reflux during 1 hr. On the following morning the *furfurylaminopyrimidine* (2·3 g.; m. p. 167—168°) was collected. Recrystallisation from alcohol gave yellow plates, m. p. 168—169° (Found: C, 48·0; H, 4·2; N, 28·6. $C_{10}H_{11}O_3N_5$ requires C, 48·2; H, 4·4; N, 28·1%).

2 : 5-Diamino-4-furfurylamino-6-methylpyrimidine.—2-Amino-4-furfurylamino-6-methyl-5-nitropyrimidine (1·6 g.) in methanol (100 ml.) was hydrogenated over Raney nickel at room temperature and pressure. After filtration from the catalyst, the solvent was removed and the residue (1·1 g.) was dried on a porous tile. Recrystallisation from toluene (carbon) gave the *diaminopyrimidine* as rhombs, m. p. 123—124° (Found: C, 55·0; H, 6·0; N, 31·7. $C_{10}H_{13}ON_5$ requires C, 54·8; H, 5·9; N, 32·0%).

2-Amino-9-furfuryl-6-methylpurine.—2 : 5-Diamino-4-furfurylamino-6-methylpyrimidine (15 g.), acetic anhydride (100 ml.), and ethyl orthoformate (100 ml.) were heated under reflux during 1 hr. Excess of reagent was removed under diminished pressure and the residue was then treated with 2·5N-sodium hydroxide (100 ml.) and ethanol (50 ml.) at 40° during 15 min. After cooling, the solid was collected and washed with water. Recrystallisation from aqueous

alcohol gave the *purine* (6·2 g.) as needles, m. p. 113—114° (Found: C, 56·7; H, 5·5; N, 29·6. $C_{11}H_{11}ON_5,0{\cdot}25H_2O$ requires C, 56·6; H, 5·0; N, 29·95%).

2-*Amino*-1′-*furfuryl*-6-*methyl*-1′ : 2′ : 3′-*triazolo*(5′ : 4′-4 : 5)*pyrimidine*.—Sodium nitrite (1·24 g.) in water (10 ml.) was added to a solution of 2 : 5-diamino-4-furfurylamino-6-methylpyrimidine (3·73 g.) in acetic acid (100 ml.) at 10°. After 10 min. the solution was added to water (500 ml.), and the *triazolopyrimidine* (3·7 g., m. p. 150—152°) was collected and washed with water. It crystallised from water in needles, m. p. 153° (Found: C, 52·1; H, 4·5; N, 36·3. $C_{10}H_{10}ON_6$ requires C, 52·2; H, 4·35; N, 36·5%).

I am grateful to Mr. K. Jones for technical assistance.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, PHARMACEUTICALS DIVISION,
ALDERLEY PARK, MACCLESFIELD, CHESHIRE. [*Received, August 11th*, 1958.]

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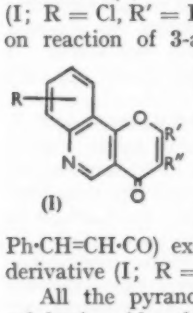
100. *Pyranoquinolines. Part I. Application of the Kostanecki–Robinson Reaction to Derivatives of 3-Acetyl-4-hydroxyquinoline.*

By K. ELLIOTT and E. TITTENSOR.

The synthesis and some reactions of certain pyranoquinolines are described.

WE have found that Snyder and Jones's method [1] for the synthesis of substituted ethyl α-acetyl-β-anilinoacrylates leads to the simultaneous formation of the corresponding acrylanilides which have not previously been recorded. Thermal cyclisation of the anilinoacrylates in an inert solvent [1,2] yielded derivatives of 3-acetyl-4-hydroxyquinoline which were heated with various acid anhydrides and the sodium salts of the corresponding acid (Kostanecki–Robinson reaction [3]). It was not possible to isolate any products from these reactions, but substitution of triethylamine [4] for the sodium salts led to a series of 4′-oxopyrano(3′ : 2′-3 : 4)quinolines (I). Interaction of benzoic anhydride and 3-acetyl-4-hydroxy-6-, -7-, or -8-nitroquinoline gave in each case a mixture of the nitro-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)quinoline (I; R = NO_2, R′ = Ph, R″ = H) and the 5′-benzoyl derivative (I; R = NO_2, R′ = Ph, R″ = Bz). A mixture of the phenylpyranoquinoline (I; R = Cl, R′ = Ph, R″ = H) and 3-acetyl-4-benzoyloxy-7-chloroquinoline was obtained on reaction of 3-acetyl-7-chloro-4-hydroxyquinoline with benzoic anhydride, whereas 3-acetyl-6-bromo-4-hydroxyquinoline yielded only the phenylpyranoquinoline (I; R = Br, R′ = Ph, R″ = H). Furoic anhydride with the above-mentioned nitro-, chloro-, and bromo-compounds gave only the 5′-furoyl derivatives of the furylpyranoquinolines (I; R = NO_2, Cl, or Br, R′ = C_4H_3, R″ = C_4H_3·CO) in all cases. Cinnamic anhydride also gave the 5′-cinnamoyl derivatives of the styrylpyranoquinolines (I; R = NO_2, Cl, or Br, R′ = Ph·CH=CH, R″ = Ph·CH=CH·CO) except that 3-acetyl-4-hydroxy-7-nitroquinoline gave only the 6′-styryl derivative (I; R = NO_2, R′ = Ph·CH=CH, R″ = H).


(I)

All the pyranoquinolines described gave characteristic colours with concentrated sulphuric acid, pale yellow in the phenyl, orange in the furyl, and deep red in the styryl series. No colours were obtained with ferric chloride in alcohol. The carbonyl group is less reactive than in the flavones and attempts to prepare oximes or 2 : 4-dinitrophenylhydrazones were unsuccessful.

[1] Snyder and Jones, *J. Amer. Chem. Soc.*, 1946, **68**, 1253.
[2] Hapara and Desai, *J. Indian Chem. Soc.*, 1954, **31**, 951—956.
[3] Allan and Robinson, *J.*, 1924, **125**, 2192.
[4] Kuhn and Law, *Ber.*, 1944, **77**, 196.

Experimental

α-Acetyl-β-p-bromoanilino-N-p-bromophenylacrylamide and Ethyl α-Acetyl-β-p-bromoanilinoacrylate.—Equimolecular quantities of ethyl orthoformate, ethyl acetoacetate, and *p*-bromoaniline were heated at 160—165° (oil-bath) in an apparatus for fractional distillation. After the theoretical amount of ethyl alcohol had distilled, the cooled solidified residue was boiled with methyl alcohol, and the insoluble material was collected from the hot mixture and crystallised from toluene, to give *α-acetyl-β-p-bromoanilino-N-p-bromophenylacrylamide* (39·8 g.) as needles, m. p. 188—189° (Found: C, 46·8; H, 3·3; N, 6·3. $C_{17}H_{14}O_2N_2Br_2$ requires C, 46·6; H, 3·2; N, 6·4%).

Further material was collected from the cooled filtrate and recrystallised from methyl alcohol, to give *ethyl α-acetyl-β-p-bromoanilinoacrylate* (135 g.) as needles, m. p. 89—91° (Found: C, 50·0; H, 4·5; N, 4·5. $C_{13}H_{14}O_3NBr$ requires C, 50·1; H, 4·4; N, 4·7%).

Similarly, *o*-nitroaniline gave *ethyl α-acetyl-β-o-nitroanilinoacrylate*, m. p. 107—109° (Found: C, 56·5; H, 5·0; N, 10·5. $C_{13}H_{14}O_5N_2$ requires C, 56·0; H, 5·0; N, 10·1%), and *α-acetyl-β-o-nitroanilino-N-o-nitrophenylacrylamide*, needles, m. p. 233—235° (Found: C, 55·6; H, 3·9; N, 15·6. $C_{17}H_{14}O_6N_4$ requires C, 55·2; H, 3·9; N, 15·1%).

The following new acrylanilides were also isolated: *α-acetyl-β-m-chloroanilino-N-m-chlorophenyl-*, m. p. 151—152° (Found: C, 59·0; H, 4·2; N, 7·9. $C_{17}H_{14}O_2N_2Cl_2$ requires C, 58·5; H, 4·0; N, 8·0%), *α-acetyl-β-m-nitroanilino-N-m-nitrophenyl-*, m. p. 188—190° (Found: C, 54·9; H, 3·6%), and *α-acetyl-β-p-nitroanilino-N-p-nitrophenyl-acrylamide*, m. p. 245—246° (Found: C, 54·9; H, 4·0; N, 15·0%).

3-Acetyl-6-bromo-4-hydroxyquinoline.—To stirred diphenyl ether (50 c.c.) at the b. p. but no longer heated, ethyl α-acetyl-β-*p*-bromoanilinoacrylate (10 g.) was added portionwise. The whole was heated under reflux for 30 min. The cooled mixture was diluted with an equal volume of ether, and the insoluble material collected and dissolved in one equivalent of dilute sodium hydroxide solution. Acidification gave *3-acetyl-6-bromo-4-hydroxyquinoline* (4·25 g.), m. p. >300° (Found: C, 49·6; H, 3·1; N, 5·5. $C_{11}H_8O_2NBr$ requires C, 49·6; H, 3·0; N, 5·3%).

6-Bromo-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)quinoline.—3-Acetyl-6-bromo-4-hydroxyquinoline (2·66 g.) was refluxed with triethylamine (6·06 g.) and benzoic anhydride (11·3 g.) at 170—180° for 3 hr., the cooled mixture extracted with ether (4 × 50 c.c.), and the insoluble material (2·2 g.) crystallised from acetic acid, to give *6-bromo-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)quinoline* (2·5 g.), needles, m. p. 228—229° (Found: C, 61·2; H, 3·0; N, 4·3. $C_{18}H_{10}O_2NBr$ requires C, 61·4; H, 2·8; N, 4·0%). The *picrate* had m. p. 260—261° (Found: N, 9·6. $C_{24}H_{13}O_9N_4Br$ requires N, 9·6%).

7-Chloro-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)quinoline.—3-Acetyl-7-chloro-4-hydroxyquinoline (3·5 g.) was refluxed with benzoic anhydride (18·0 g.) and triethylamine (9·6 g.) at 170—180° for 4·25 hr., the cooled mixture extracted with ether (4 × 50 c.c.), and the insoluble material (4·3 g.) boiled with ethyl alcohol (300 c.c.) for 15 min. The residue (0·8 g.) crystallised from glacial acetic acid, giving *3-acetyl-4-benzoyloxy-7-chloroquinoline*, needles, m. p. 245—246° (Found: C, 65·9; H, 3·8; N, 3·8. $C_{18}H_{12}O_3NCl$ requires C, 66·4; H, 3·7; N, 4·3%).

The alcoholic filtrate was concentrated, to give *7-chloro-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)-quinoline* (3·3 g.), needles, m. p. 203—204° (Found: C, 70·8; H, 3·3; N, 4·0. $C_{18}H_{10}O_2NCl$ requires C, 70·3; H, 3·3; N, 4·5%).

Similarly, 3-acetyl-4-hydroxy-6-nitroquinoline at 150—160° (3·5 hr.), and the corresponding -7- and -8-nitroquinolines at 170—180° (3·0 and 2·0 hr., respectively), gave mixtures of the following ether-insoluble pyranoquinolines: *5′-benzoyl-6-nitro-*, prisms (from acetic acid), m. p. 249—250° (decomp.) (Found: C, 70·9; H, 3·4; N, 6·8. $C_{25}H_{14}O_5N_2$ requires C, 71·1; H, 3·3; N, 6·6%), *6-nitro-*, prisms (from) ethyl alcohol), m. p. 268—270° decomp.) (Found: C, 67·4; H, 3·2; N, 8·8. $C_{18}H_{10}O_4N_2$ requires C, 67·9; H, 3·2; N, 8·8%) [methiodide, m. p. 188° (decomp.) (Found: N, 5·8. $C_{19}H_{13}O_4N_2I$ requires N, 6·1%) (separated from the 5′-benzoyl derivative by extraction with hot alcohol), *5′-benzoyl-7-nitro-*, prisms (from acetone), m. p. 282° (decomp.) (Found: C, 70·8; H, 3·4; N, 6·8%), *7-nitro-*, prisms (from nitrobenzene), m. p. 285—287° (decomp.) (Found: C, 67·7; H, 2·8; N, 9·2%) (separated from the 5′-benzoyl derivative by extraction with hot methyl alcohol), *5′-benzoyl-8-nitro-*, prisms (from *n*-propyl alcohol), m. p. 192° (Found: C, 70·4; H, 3·2; N, 6·6%), and *8-nitro-*, prisms [from 1 : 1 ethyl acetate–light

petroleum (b. p. 40—60°)], m. p. 222—225° (decomp.) (Found: C, 68·2; H, 3·3; N, 8·8%) (separated from the 5′-benzoyl derivative by extraction with hot toluene) *4′-oxo-6′-phenylpyrano*-(3′ : 2′-3 : 4)*quinoline*.

6-Bromo-5′-furoyl-6′-furyl-4′-oxopyrano(3′ : 2′-3 : 4)*quinoline*.—3-Acetyl-6-bromo-4-hydroxyquinoline (2·66 g.), triethylamine (11·1 g.), and furoic anhydride (10·3 g.) were refluxed at 170—180° for 3·5 hr. Extraction of the resultant black oil with acetone gave *6-bromo-5′-furoyl-6′-furyl-4-oxopyrano*(3′ : 2′-3 : 4)*quinoline* (3·2 g.), needles (from nitrobenzene), m. p. >300° (Found: C, 57·6; H, 2·5; N, 3·8. $C_{21}H_{10}O_5NBr$ requires C, 57·8; H, 2·3; N, 3·2%).

Similarly, 3-acetyl-7-chloro-4-hydroxyquinoline, 3-acetyl-4-hydroxy-6-, -7-, and -8-nitroquinoline gave: the *7-chloro-* (prepared at 160—170°; 2·5 hr.), needles (from nitrobenzene), m. p. >300° (Found: C, 64·3; H, 2·4; N, 3·9. $C_{21}H_{10}O_5NCl$ requires C, 64·4; H, 2·6; N, 3·6%), *6-nitro-* (prepared at 170—180°; 2 hr.), prisms (from nitrobenzene), m. p. 228° (decomp.) (Found: C, 62·2; H, 2·7; N, 7·3. $C_{21}H_{10}O_7N_2$ requires C, 62·7; H, 2·5; N, 7·0%), *-7-nitro-* (prepared at 150—160°; 2·5 hr.), prisms (from nitrobenzene), m. p. >300° (Found: C, 62·9; H, 2·5; N, 7·3%), and *8-nitro-derivative* (prepared at 160—170°; 2·5 hr.), needles (from nitrobenzene), m. p. >300° (Found: C, 63·1; H, 2·7; N, 7·5%), of *5′-furoyl-6′-furyl-4′-oxopyrano*-(3′ : 2′-3 : 4)*quinoline*.

6-Bromo-5′-cinnamoyl-4′-oxo-6′-styrylpyrano(3′ : 2′-3 : 4)*quinoline*.—3-Acetyl-6-bromo-4-hydroxyquinoline (2·66 g.) was refluxed with cinnamic anhydride (13·9 g.) and triethylamine (6·06 g.) at 170—180° for 3·25 hr. The resultant black oil was kept at room temperature for 2 days, then diluted with acetone (25 c.c.), and the insoluble material crystallized from dioxan to give *6-bromo-5′-cinnamoyl-4′-oxo-6′-styrylpyrano*(3′ : 2′-3 : 4)*quinoline* as needles, m. p. 271—273° (decomp.) (Found: C, 68·2; H, 3·7; N, 3·3. $C_{29}H_{18}O_3NBr$ requires C, 68·5; H, 3·6; N, 2·8%).

Similarly were prepared *7-chloro-5′-cinnamoyl-* (at 170—180°; 3·5 hr.), prisms (from *n*-butyl alcohol), m. p. 250° (Found: C, 74·7; H, 4·3; N, 2·3. $C_{29}H_{18}O_3NCl$ requires C, 75·1; H, 3·9; N, 2·9%), *5′-cinnamoyl-6-nitro-* (160—170°; 3·0 hr.), needles (from nitrobenzene), m. p. 250° (decomp.) (Found: C, 72·7; H, 4·0; N, 6·2. $C_{29}H_{18}O_5N_2$ requires C, 73·4; H, 3·8; N, 5·9%), *7-nitro-* (160—170°; 2 hr.), prisms (from nitrobenzene), m. p. 288° (decomp.) (Found: C, 70·0; H, 3·8; N, 6·9. $C_{20}H_{12}O_4N_2$ requires C, 69·8; H, 3·5; N, 7·1%), and *5′-cinnamoyl-8-nitro-4′-oxo-6′-styrylpyrano*(3′ : 2′-3 : 4)*quinoline* (160—170°; 2·5 hr.), prisms (from acetic acid), m. p. 236° (decomp.) (Found: C, 73·5; H, 3·8; N, 5·7%).

Alkaline Hydrolysis of 6-Bromo- and 8-Nitro-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)*quinoline*.—6-Bromo-4′-oxo-6′-phenylpyrano(3′ : 2′-3 : 4)quinoline (0·2 g.) was refluxed in 0·1N-sodium hydroxide (10 c.c.) and ethyl alcohol (2 c.c.) for 1·5 hr. The cooled mixture, on extraction with ether (10 c.c.), gave acetophenone (0·05 g.) (2 : 4-dinitrophenylhydrazone, m. p. 238—240°). Acidification of the aqueous phase afforded *3-bromo-4-hydroxyquinoline-3-carboxylic acid* (0·13 g.), m. p. 276° (decomp.) (Found: N, 5·2. $C_{10}H_6O_3NBr$ requires N, 5·2%).

Similarly the nitro-compound (0·2 g.) gave acetophenone (0·05 g.) and *8-nitroquinoline-3-carboxylic acid* (0·25 g.), m. p. 264° (Found: N, 11·6. $C_{10}H_6O_5N_2$ requires N, 12·0%).

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101. *Polynitronaphthalenes. Part II.*[1] *A Quantitative Study of the Nitration of* 1- *and* 2-*Nitronaphthalene and of* 1 : 5-*Dinitronaphthalene.*

By E. R. Ward, C. D. Johnson, and (in part) L. A. Day.

Methods are described for the application of column and paper chromatography, and complex formation, to the detection, separation, and estimation of products arising from the nitration of 1- and 2-nitronaphthalene and of 1 : 5-dinitronaphthalene. The influence of nitration medium, temperature, and added catalyst has been studied in appropriate cases. Significant differences have been found between sulphuric and aqueous nitric acids as media, and these are discussed in relation to current theories of aromatic nitration, particularly the dipolar influences of the nitro-group (the *D*-effect of Ward and Wells [2]).

1 : 3 : 5 : 7-Tetranitronaphthalene is identified for the first time as a nitration product of 1 : 5-dinitronaphthalene. Improved and convenient preparative methods for 1 : 3 : 5- and 1 : 4 : 5-trinitronaphthalene, and for 1 : 3 : 5 : 8-, 1 : 3 : 5 : 7-, and 1 : 4 : 5 : 8-tetranitronaphthalene are described. The last can be prepared directly from 1-nitronaphthalene and is thus made readily available for the first time.

Since the nitration of naphthalene has been studied for over a hundred years it is rather surprising that all the polynitronaphthalenes that can thereby be formed have not yet been identified and that reasonably accurate determinations of the proportions of isomers formed have only been made in the case of mononitration. The completion of the present investigation leaves only the products arising from 1 : 7-dinitronaphthalene (*via* 2-nitronaphthalene) to be precisely identified and estimated, although preliminary studies of this have been made.[3,4] The present work is essentially a continuation of that of Hodgson and Ward [1] and will be completed by a quantitative study of the nitration of all ten dinitronaphthalenes. The results of the present investigation are summarised in Table 1.

In a previous communication [5] we have pointed out that the proportions of 1 : 5- and 1 : 8-dinitronaphthalene arising from the nitration of 1-nitronaphthalene in sulphuric acid have never been accurately determined and that indeed this ratio might not be 2 : 1, as it has always been assumed to be. However, we have now avoided the complications due to concurrent formation of trinitronaphthalenes (cf. Ward and Hawkins [6]) and shown that for nitrations at 0°, to a very high degree of accuracy, the ratio can be taken as exactly 2 : 1.

No satisfactory explanation has ever been given why the 8-position should be so much favoured over the alternative 5-position in this nitration, when one would have expected on steric grounds that the reverse would apply. Wells and Ward [2] (cf. Hammond *et al.*[7]) have discussed this in relation to the general problem of dipole influences in aromatic substitution, and concluded that it can be satisfactorily explained in terms of the favourable orientation of the substituent dipole to the incoming positively charged nitronium ion, thus reducing the deactivating influence of the α-nitro-group at the 8-position. They have suggested that such dipolar influences be considered as a specific reactivity-determining influence, the *D*-effect. For nitrations in aqueous nitric acid the definite increase in 5-substitution could be ascribed to the fact that an increase in reagent size (the effective

[1] Part I, Hodgson and Ward, *J.*, 1946, 533.
[2] Wells and Ward, *Chem. and Ind.*, 1958, 1172.
[3] Day, Thesis, London, 1952.
[4] Ward and Hawkins, unpublished work.
[5] Ward, *Chem. and Ind.*, 1956, 195.
[6] Ward and Hawkins, *J.*, 1954, 2975.
[7] Hammond, Modic and Hedges, *J. Amer. Chem. Soc.*, 1953, **75**, 1388.

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agent in this medium probably being the hydrated nitronium ion $H_2NO_3^+$, cf. Halberstadt, Hughes, and Ingold [8]) may bring about greater steric hindrance at the 8-position.

Unfortunately, the situation is complicated by the claim of Bachman *et al.*[9,10] (cf. Ward [5]) that nitration of naphthalene by the boron trifluoride–nitrogen tetroxide complex in nitroethane at 80° produces a mixture of 1 : 5- and 1 : 8-dinitronaphthalene in a ratio of *ca.* 1·5 : 1 (cf. our nitration in sulphuric acid containing boron trifluoride). The claim being accepted at its face value, it is a remarkable result and one can only tentatively

TABLE 1. *Nitration of* 1- *and* 2-*nitronaphthalene*, 1 : 5-*dinitronaphthalene, and* 1 : 3 : 5- *and* 1 : 4 : 5-*trinitronaphthalene.*

Nitro-compound	Nitration conditions	HNO_3 (mole)	Yield (%)	Product composition * (%)	Analysis
1	A1, 0°	1	98·1	1 : 5, 33·5; 1 : 8, 66·5 *†	C
1	A2, 0°	0·7	98·3	1 : 5, 33·3; 1 : 8, 66·7 *†	C
1	A3, −40°	0·85	—	1 : 5, 32·4; 1 : 8, 67·6 †‡	C
1	B1	X	93·7	1 : 5, 37·2; 1 : 8, 56·5; T, 6·3	C
			93·3	1 : 5, 38·6; 1 : 8, 54·7; T, 6·1	C
2	A1, −5°	0·5	99·6	1 : 6, 41 ± 1; 1 : 7, 59 ± 1	C
1 : 5	A4, 30°	1·5	93·5	1 : 4 : 5, 94; 1 : 3 : 5, 6	C, S, P
1 : 5	B1	X	52	1 : 4 : 5, 34; 1 : 3 : 5, 47; 1 : 3 : 5 : 7, 19	M
1 : 5	B2	X	38	1 : 4 : 5, 48; 1 : 3 : 5, 49; 1 : 3 : 5 : 7, 3	M, P
1 : 5	B3	X	71	1 : 4 : 5, 92; 1 : 3 : 5, 8	M
1 : 5	A4, 80°	14	51	1 : 4 : 5 : 8, 53; 1 : 3 : 5 : 8, 47	SL, P
1 : 3 : 5	A4, 80°	25	60	1 : 3 : 5 : 8	
1 : 3 : 5	B3	X	42	1 : 3 : 5 : 7	P
1 : 4 : 5	A4, 90°	14	37	1 : 4 : 5 : 8, 67; 1 : 3 : 5 : 8, 33	SL
1 : 4 : 5	B3	X	51	1 : 3 : 5 : 8	

The initial compound and nitration products are described by the position of the nitro-groups in the naphthalene nucleus.

Nitration conditions. A1, sulphuric acid (*d* 1·84)–nitric acid (*d* 1·42). A2, sulphuric acid (*d* 1·84)–nitric acid (*d* 1·5)–boron trifluoride–acetic acid. A3, sulphuric acid (*d* 1·84)–nitric acid (*d* 1·42)–acetic anhydride. A4, sulphuric acid (*d* 1·84)–nitric acid (*d* 1·5). B1, 70% w/w aqueous nitric acid (reflux). B2, 85% w/w aqueous nitric acid (reflux). B3, 92·5% w/w aqueous nitric acid (reflux). X = Excess.

Yield. For the mononitronaphthalenes this represents the proportion of the nitration product (including unchanged reactant) recovered by chromatography. For the remainder this represents the yield of polynitronaphthalenes isolated from the nitration product in relation to the original reactant and the degree of nitration achieved.

* Calculated on the isolated polynitronaphthalenes.

† Accurate to ±0·2%, losses on chromatography being assumed to be due to oxidation products only.

‡ Mean of two determinations, within 0·2% of each other.

T, Trinitronaphthalenes. C, Column chromatography. P, Paper chromatography. S, Infrared spectroscopy. M, Molecular complex formation. SL, Solvent separation.

suggest that it might be explained in terms of a much increased reagent size greatly reducing reactivity at the usually favoured 8-position.

The composition of the product is accurately given for the first time for the nitration of 2-nitronaphthalene and again it is suggested that the preferential substitution at the 8-position can be explained by the *D*-effect, weakened in this case by the less favourable position of the β-nitro-group, but counterbalanced to some extent by the decrease in steric hindrance at the 8-position. Thus the *D*-effect can only operate at an *ortho*-position in benzene, but in naphthalene it can operate in several ways, two of which we have already illustrated, and another of the original Hammond type manifested by the formation of 1 : 2 : 4 : 6- and 1 : 2 : 6 : 8-tetranitronaphthalenes in the dinitration of 2 : 6-dinitronaphthalene.[11]

The nitration of 1 : 5-dinitronaphthalene both in sulphuric acid and in aqueous nitric

[8] Halberstadt, Hughes, and Ingold, *J.* 1950, 2441.
[9] Bachman, Feuer, Bleustein, and Vogt, *J. Amer. Chem. Soc.*, 1955, **77**, 6188.
[10] Bachman and Vogt, *J. Amer. Chem. Soc.*, 1958, **80**, 2381.
[11] Chatt and Wynne, *J.*, 1943, 32.

acid medium has been studied by various workers. Qualitatively this work [12-15] demonstrated the formation of 1 : 4 : 5-trinitro- and of 1 : 3 : 5 : 8- and 1 : 4 : 5 : 8-tetranitronaphthalene in sulphuric acid, and that of 1 : 3 : 5- and 1 : 4 : 5-trinitronaphthalene in nitric acid medium; Pascal's claim [16] to have obtained 1 : 3 : 5-trinitronaphthalene in sulphuric acid is considered unreliable. Detailed examination of the published work [3] showed that of Dimroth and Ruck [15] to be apparently the most reliable. A comprehensive reinvestigation was clearly indicated.

Qualitatively, we have shown that 1 : 3 : 5-trinitronaphthalene is a minor product of nitration in sulphuric acid, and have identified 1 : 3 : 5 : 7-tetranitronaphthalene as a nitration product in aqueous nitric acid (it could not be detected even by paper chromatography for nitration in sulphuric acid). We have made reasonably accurate determinations of the composition of the nitration products, this being important for interpretative purposes. We have also devised more satisfactory preparative methods for the various nitration products. 1 : 4 : 5 : 8-Tetranitronaphthalene can now be made directly from 1-nitronaphthalene instead of through 1 : 5-dinitronaphthalene (involving separation from 1 : 8-dinitronaphthalene). 1 : 3 : 5 : 7-Tetranitronaphthalene was previously only available by nitration of the difficultly accessible 2 : 6-dinitronaphthalene. 1 : 3 : 5-Trinitronaphthalene is made more accessible by decomposition of its complex with 2-naphthol on alumina.

Our nitration results for 1 : 5-dinitronaphthalene can be given a satisfactory explanation. The operation of the *D*-effect favours the formation of 1 : 4 : 5-trinitronaphthalene as against the alternative 1 : 3 : 5-isomer for mononitration in sulphuric acid, whereas in aqueous nitric acid increase in reagent size increases the relative amount of 1 : 3 : 5-isomer, the latter being complicated by the fact that the stronger aqueous nitric acid will contain an increased amount of the nitronium ion. In the further nitration of 1 : 4 : 5-trinitronaphthalene a possible complicating effect is the presence of the adjacent nitro-groups at the 4- and the 5-position. These must sterically interfere with one another and consequently be forced out of the plane of the rings. This may therefore aid substitution in the superficially deactivated 8-position but again the issue seems to turn on the favouring *D*-effect from the 1-nitro-group giving predominant substitution at the 8- rather than the 7-position. The formation of 1 : 3 : 5 : 8-tetranitronaphthalene in the nitration of 1 : 4 : 5-trinitronaphthalene in aqueous nitric acid can be accounted for by increase in reagent size. The nitrations of 1 : 3 : 5-trinitronaphthalene are not complicated by steric factors and are straightforward in terms of the above ideas. It must be borne in mind that nitration in aqueous nitric acid is complicated by attendant oxidation and renders the results less susceptible to precise interpretation.

Experimental

Column Chromatography: General Technique and Separation of Synthetic Mixtures.—An alumina column was prepared by using 1 : 1 benzene–light petroleum (b. p. 40—60°) as solvent medium, and the mixed polynitronaphthalenes were applied to this in solution in benzene, elution also being by benzene. The eluate was collected in small fractions (varied according to the nature of the separation as determined by a preliminary trial); each fraction was concentrated to small volume and evaporated to dryness. The progress of the separation was largely followed from the weights and m. p.s of the eluted products rather than by the appearance of the column during elution. In all cases a slight pink or yellow band appeared at the top of the column; dinitronaphthalenes may give pale yellow bands but trinitro- and tetranitronaphthalenes tend to give a red or intense red colour to the whole column. These colours appeared to be due to decomposition brought about both by the alumina and by the photosensitivity of the nitro-compounds when on the column. Although they may aid in following

[12] de Aguiar, *Ber.*, 1872, **5**, 370, 897.
[13] Beilstein and Kuhlberg, *Annalen*, 1873, **169**, 81.
[14] Will, *Ber.*, 1895, **28**, 367.
[15] Dimroth and Ruck, *Annalen*, 1926, **446**, 123.
[16] Pascal, *Bull. Soc. chim.* (*France*), 1920, **27**, 388.

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the separation, it is best to reduce the exposure of the column to light to a minimum, and furthermore it was not found that irradiation by ultraviolet light was of any assistance in detecting the bands. The decomposition that occurs on the column is negligible with mono- or di-nitronaphthalenes but may become appreciable with some trinitronaphthalenes and is excessive, producing quantities of coloured intractable tars, from tetranitronaphthalenes. Other absorbents such as neutralised alumina, magnesium oxide, or silica gave less colour or decomposition but were not satisfactory for separative purposes. In the chromatography of actual nitration products it appears that the by-products are usually much more strongly adsorbed on the column and tend to remain at the top of it until, following the elution of the actual nitro-compounds, powerful eluting solvents (*e.g.*, ethyl acetate) are applied to remove them. The method appears to be capable of separating favourable mixtures with an accuracy as high as $\pm 0{\cdot}2\%$.

(a) 1 : 8- *and* 1 : 5-*Dinitronaphthalene*. A mixture of 1 : 5- (0·299 g.) and 1 : 8-dinitronaphthalene (0·301 g.), dissolved in benzene (100 c.c.), was poured on alumina (35 × 3 cm.). The first 11 fractions (×100 c.c.) contained only 1 : 5-dinitronaphthalene, the next was free from nitro-compounds, and subsequent elution was by ethyl acetate, the 1 : 8-dinitronaphthalene being completely eluted in fractions 14—19. Recovery of the 1 : 5-isomer was 0·298 g. and that of the 1 : 8-isomer 0·301 g., the overall recovery being 99·8%.

(b) 1 : 6- *and* 1 : 7-*Dinitronaphthalene*. 1 : 6- (0·196 g.) and 1 : 7-Dinitronaphthalene (0·201 g.) were used on alumina (40 × 2·5 cm.). A yellow band appeared on the column and later split into two: by the time the lower, yellow band (corresponding to the 1 : 7-isomer, the 1 : 6-isomer giving no colour) had been eluted the other was about halfway down the column; 50 c.c. fractions were taken, the first ten were solvent only, the next four gave pure 1 : 6-isomer (0·144 g.), the next four gave mixed isomers (0·179 g.), and the next six pure 1 : 7-isomer (0·082 g.). The mixed isomers were dissolved in 1 : 1 benzene–light petroleum and rechromatographed. The 6th and 7th fractions gave pure 1 : 6-isomer, the next three gave mixed isomers, and the next ten gave pure 1 : 7-isomer. This procedure was repeated again with the mixed isomers and these decreased to *ca.* 0·003 g. (*ca.* 1% of original mixture). Recovery of the 1 : 6-isomer was 0·190 g. (97%) and of the 1 : 7-isomer 0·203 g. (100%).

(c) 1 : 3 : 8- *and* 1 : 4 : 5-*Trinitronaphthalene*. A 1 : 1 mixture (0·60 g.) on alumina (40 × 4 cm.) was used. The 1 : 4 : 5-isomer was quantitatively recovered from the first ten fractions (×100 c.c.) and the 1 : 3 : 8-isomer (98·2%) in the next five. The red coloration of the column and tar found in the final fractions appeared to be due to decomposition of the 1 : 3 : 8-isomer.

Paper Chromatography: General Technique and Accuracy of Method (*With* L. A. Telesz).—The paper chromatography was largely carried out by the method due to Franc and Latinák.[17] Strips of Whatman No. 4 paper, of sufficient width to accommodate five separations at 1·5 in. apart, and with the machine direction running vertically, were impregnated with petroleum distillate (Shell distillate: boiling range 190—275°) by dipping them first in the pure solvent, and then in a 9 : 1 mixture of benzene–petroleum distillate, and allowing the benzene to evaporate off.

The polynitronaphthalene mixtures were applied to the paper in acetic acid–pyridine or acetone (0·25—0·5% w/v solutions, depending on the composition of, and the number of components in, the mixture). The chromatogram was developed by downward displacement, elution being with ethanol–water–acetic acid (20 : 14 : 1 by vol.) for *ca.* 8 hr., during which the front traversed a distance of *ca.* 25 cm. The temperature was kept at 21° ± 1° throughout.

After the chromatogram had been dried, the individual nitronaphthalenes were faintly visible as brown, red, or yellow spots, and clearly visible as black or blue fluorescent spots under ultraviolet light.

The size of an individual spot in a mixture appeared to have no correlation with the proportion of that substance in the mixture, and the method was therefore used mainly as a qualitative procedure. However, in 1 : 3 : 5- and 1 : 4 : 5-trinitronaphthalene mixtures referred to later, the amount of each isomer present appeared to be approximately equal to the area of the spot. A semi-quantitative result was obtained in this case by comparing the areas and intensities of the spots with those from a standard 1 : 1 mixture of 1 : 3 : 5- and 1 : 4 : 5-trinitronaphthalene and with spots of the individual isomers of known concentration.

Mononitration of α-Nitronaphthalene.—(*a*) The nitro-compound (4·0 g.) was nitrated as described by Ward and Hawkins,[6] care being taken to avoid all dinitration. The yield was

[17] Franc and Latinák, *Chem. Listy*, 1955, **49**, 872.

5·04 g. (100% for mononitration). In the subsequent chromatography (1·049 g.; alumina column, 40 × 3·5 cm.) 100 c.c. fractions were collected; pure 1 : 5-dinitronaphthalene (0·323 g.) appeared in fractions 4—9, fractions 10 and 11 gave 0·042 g. of mixed isomers, and the remainder was pure 1 : 8-isomer, no trinitronaphthalenes being found. After rechromatography of the mixed isomers the overall recovery was 98·1%. Brown and yellow bands remained at the top of the column after the nitro-compounds had been eluted.

(*b*) The nitro-compound (2·00 g.) in sulphuric acid (*d* 1·84; 16 c.c.) was slowly treated at 0° by a mixture of nitric acid (*d* 1·5; 0·5 g., 0·68 mol.) and boron trifluoride–acetic acid complex in acetic acid (40% boron trifluoride; 15 c.c.). The nitration product was isolated as above (2·29 g.); 1·018 g. of this were chromatographed, 75 c.c. fractions being collected. Pure 1-nitronaphthalene was found in fractions 8—11, fractions 12—14 were a mixture of 1-nitronaphthalene and 1 : 5-dinitronaphthalene (separated by rechromatography), and fractions 15—24 gave pure 1 : 5-dinitronaphthalene; the 1 : 8-isomer was subsequently eluted by ethyl acetate (3 × 75 c.c.), and nothing more was obtained by further elution. The 1-nitronaphthalene gave a clear yellow band on the column and its elution was easy to follow.

(*c*) A suspension of 1-nitronaphthalene (2·00 g.) in acetic anhydride (12 c.c.) was treated at −50° to −40° with a 4 : 1 v/v mixture (3·1 c.c.) of sulphuric acid (*d* 1·84) and nitric acid (*d* 1·42) during 10 min., and after a further 10 min. the mixture poured on ice. The nitration product (2·23 g.) was separated as in (*b*).

(*d*) The 1-nitronaphthalene (2·00 g.) was warmed with nitric acid (*d* 1·42; 5 c.c.) until solution occurred and then refluxed a further 10 min. Chromatography of the nitration product gave pure 1 : 5- and 1 : 8-isomers together with intermediate fractions which appeared to be mainly 1 : 4 : 5-trinitronaphthalene. 1 : 3 : 8-Trinitronaphthalene was probably not present to any significant extent since there was no deep red colour on the column.

Mononitration of 2-Nitronaphthalene.—The nitration was carried out as in (*a*) above but at −10° to −5°. Chromatography gave first most of the unchanged 2-nitronaphthalene, then a small amount of this mixed with 1 : 6-dinitronaphthalene, then successively about equal amounts of pure 1 : 6-isomer, mixed 1 : 6- and 1 : 7-isomers, and pure 1 : 7-isomer. The mixtures were separated by rechromatography.

Trinitration of 1-Nitronaphthalene and Preparation of 1 : 4 : 5 : 8-Tetranitronaphthalene.—1-Nitronaphthalene (25 g.) in sulphuric acid (*d* 1·84; 115 c.c.) was treated with a 4 : 1 v/v mixture (45 c.c.) of sulphuric acid (*d* 1·84) and nitric acid (*d* 1·42). The temperature was allowed to rise to 30° and then nitric acid (*d* 1·5; 160 c.c.) was added, the temperature being kept below 75°. The mixture was kept at 75—90° till frothing ceased, and then heating was continued on the water-bath for 2 hr. After being kept at −5° for 30 min. the solids were collected, and washed with small portions of sulphuric acid, then thoroughly with water. The yield was 23 g. (52% as tetranitronaphthalenes). The product (11 g.) was boiled with acetone (100 c.c.), and the residual 1 : 4 : 5 : 8-tetranitronaphthalene collected (1·8 g.; 8·5% overall yield). The latter began to decompose and sublime at *ca.* 280°, finally exploding at *ca.* 360°. The acetone mother-liquor was concentrated to 30 c.c. and then treated with 2-naphthol (4 g.) whereupon its complex with 1 : 3 : 6 : 8-tetranitronaphthalene separated (7 g.). This was decomposed by boiling methanol to give almost pure 1 : 3 : 6 : 8-tetranitronaphthalene (m. p. 195°). Further concentration of the residual solvent gave material (6 g.) which could not be purified. In another attempt to develop a method for isolating the 1 : 3 : 5 : 8-tetranitronaphthalene, a synthetic mixture (1 : 1 : 4) of 1 : 3 : 5 : 8-, 1 : 4 : 5 : 8-, and 1 : 3 : 5 : 8-tetranitronaphthalene was first extracted with acetone (16 c.c./g.). This gave almost quantitative recovery of the 1 : 4 : 5 : 8-isomer but treatment of the mother-liquors with 2-naphthylamine gave a complex from which no pure isomer could be obtained on decomposition by hydrochloric acid.

Mononitration of 1 : 5-Dinitronaphthalene in Sulphuric Acid and the Preparation of 1 : 4 : 5-Trinitronaphthalene.—To a vigorously stirred suspension of 1 : 5-dinitronaphthalene (10 g.) in sulphuric acid (*d* 1·84; 50 c.c.) was added dropwise, during 15 min., nitric acid (*d* 1·5; 2·9 c.c.), the temperature not being allowed to rise above 30°. After being stirred for 3 hr. more, the mixture was poured on crushed ice, and the solids were collected, thoroughly washed, and dried *in vacuo* at 60° (11·9 g.). Pure 1 : 4 : 5-trinitronaphthalene (m. p. 147—149°) was obtained by dissolving this product in hot benzene (10 c.c./g.) and collecting the solids after storage overnight (8·5 g. from 10 g.; *ca.* 80% overall yield). A portion of the filtrate (containing 0·33 g. of solute) was examined by chromatography on alumina (20 × 2·5 cm.). A deep red band was immediately formed at the head of the column and then rapidly moved

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down until the whole column was of uniform colour. The eluted product, however, was pale yellow. No nitro-compounds were eluted until the red band had reached the bottom of the column and all the subsequent fractions contained mainly 1 : 3 : 5-trinitronaphthalene, the later fractions being contaminated with a little 1 : 4 : 5-isomer; the m. p.s ranged from 101° to 119°, the latter being that of pure 1 : 3 : 5-trinitronaphthalene (Ward, Hardy, and Coulson [18] give m. p. 119—121°). The weights and m. p.s of the various fractions indicated a ratio of 19 : 1 for 1 : 4 : 5- to 1 : 3 : 5-trinitronaphthalene in the original nitration product, this being confirmed by infrared spectroscopy or paper chromatography, which indicated limits of ±2%.

Dinitration of 1 : 5-*Dinitronaphthalene in Sulphuric Acid, and the Preparation of* 1 : 3 : 5 : 8-*Tetranitronaphthalene.*—A suspension of 1 : 5-dinitronaphthalene (10 g.) in sulphuric acid (*d* 1·84; 25 c.c.) was treated dropwise, with vigorous stirring, with nitric acid (*d* 1·5; 27 c.c.). When addition was complete the temperature was allowed to rise to 80° whereat there was considerable frothing. After 1 hr. at 80° the mixture was cooled and poured on ice, washed thoroughly with water, and dried *in vacuo* (yield 7·6 g.; 51% as tetranitronaphthalenes). This product (0·65 g.) was extracted with hot benzene (3 × 20 c.c.), affording a residue (0·24 g.) of pure 1 : 4 : 5 : 8-tetranitronaphthalene. The mother-liquors were chromatographed on a cellulose column (35 × 1·5 cm.), fractional elution being by benzene. The initial fractions (100 c.c.) contained some 1 : 4 : 5 : 8-tetranitronaphthalene (total weight 0·342 g.) which was separated from the 1 : 3 : 5 : 8-isomer by acetone or benzene extraction. The next 150 c.c. gave reddish material; from benzene this gave almost pure 1 : 3 : 5 : 8-tetranitronaphthalene, m. p. 186—192° (total 0·308 g.). Paper chromatography of solids obtained by evaporation of the original mother-liquor did not show the presence of 1 : 3 : 5 : 7-tetranitronaphthalene.

To prepare 1 : 3 : 5 : 8-tetranitronaphthalene, the nitration mixture was cooled to −5° for 30 min., and the solids were collected and washed with small amounts of ice-cold 50% w/v aqueous sulphuric acid, and then thoroughly with water. After drying *in vacuo* the solids were extracted with hot benzene or acetone (2 × 7 c.c./g.), the 1 : 4 : 5 : 8-isomer removed, and further amounts of this removed by concentration; further concentration then yielded almost pure 1 : 3 : 5 : 8-tetranitronaphthalene, m. p. 191—196°, raised by recrystallisation from hot fuming nitric acid to 194° (Will [14] gives 194—195°) (overall yield *ca.* 20%).

Nitration of 1 : 5-*Dinitronaphthalene in Aqueous Nitric Acid, and Preparation of* 1 : 3 : 5-*Trinitronaphthalene and* 1 : 3 : 5 : 7-*Tetranitronaphthalene.*—(a) *In* 70% *w/w aqueous nitric acid.* The nitro-compound (20 g.) was refluxed with the acid for 20 hr., solution being complete after 6 hr. The mixture was poured on ice, and the solid collected, thoroughly washed with water, and dried *in vacuo* (15 g.). This was extracted by boiling benzene (100 c.c.), the extract cooled, and the precipitated 1 : 3 : 5 : 7-tetranitronaphthalene collected (1·5 g., m. p. 260°). To the filtrate was added 2-naphthol (9 g.) in benzene (20 c.c.), the whole warmed and stored overnight, and the red solids collected, washed with benzene, and dried (10·2 g.). The mother-liquor was evaporated to dryness; the red product on recrystallisation from benzene (charcoal) gave pure 1 : 4 : 5-trinitronaphthalene (4·2 g.). The 2-naphthol complexes were partially separated by crystallisation from chloroform (35 c.c.); the residue was mainly that from 1 : 3 : 5 : 7-tetranitronaphthalene, and the 1 : 3 : 5-trinitronaphthalene complex was obtained from the mother-liquors. These complexes were decomposed by repeatedly boiling them with methanol until the colour disappeared. Alternatively, the 1 : 3 : 5-complex was much more satisfactorily decomposed by chromatography in benzene on alumina. The 2-naphthol forms a bright red band at the top of the column, the 1 : 3 : 5-trinitronaphthalene giving a pale red colour to the column (recovery *ca.* 85%). A similar experiment was carried out in 85% w/w aqueous nitric acid.

(b) *In* 92·5% *w/w nitric acid.* The nitro-compound (20 g.) was intimately mixed with water (10 c.c.) and then treated with nitric acid (*d* 1·5, 100 c.c.), whereupon it immediately dissolved. The solution was refluxed for 12 hr. and poured on ice, and the solid collected, thoroughly washed with water, and dried (20·5 g.). This (15 g.) was dissolved in hot benzene, and overnight almost pure 1 : 4 : 5-trinitronaphthalene was deposited, further small amounts being obtained by concentration of the filtrate (total 12·5 g.). The mother-liquor was mixed with a solution of 2-naphthol (3 g.) in benzene (50 c.c.), the mixture warmed, and the complex subsequently separated, further amounts being obtained by concentration. After decomposition on alumina the yield of 1 : 3 : 5-trinitronaphthalene was 1·04 g. The losses almost certainly represent oxidation products formed during nitration.

[18] Ward, Hardy, and Coulson, *J.*, 1957, 2634.

Mononitration of 1 : 3 : 5- *and* 1 : 4 : 5-*Trinitronaphthalene in* 92·5% *w/w aqueous Nitric Acid.*—The nitration procedure for the individual trinitronaphthalenes was as described in the previous experiment.

Formation of Molecular Complexes between Polynitronaphthalenes and 2-*Naphthol.*—The nitro-compound (1 g.) was dissolved in the minimum amount of hot chloroform and treated with a saturated solution of 2-naphthol (1 g.) in chloroform, and the solids were collected and washed with chloroform. The *complex* from 1 : 3 : 6 : 8-tetranitronaphthalene was pale orange, m. p. 205°, stable in chloroform, benzene, acetic acid, or acetone, but decomposed by hot methanol with difficulty (Found: N, 12·8. $C_{20}H_{12}O_9N_4$ requires N, 12·8%). That from 1 : 3 : 5 : 8-tetranitronaphthalene was salmon-pink, m. p. 168°, with similar properties (Found: N, 12·8%). The scarlet *complex* from 1 : 3 : 5 : 7-tetranitronaphthalene had m. p. 197°, decomposed with difficulty by hot methanol but more readily by hot acetone (Found: N, 12·8%). Complexes were not given by 1-nitronaphthalene, 1 : 2-, 1 : 3-, 1 : 4-, and 1 : 5-dinitronaphthalene, or 1 : 4 : 5-, 1 : 3 : 6-, or 1 : 3 : 8-trinitronaphthalene.

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102. *Red-seaweed Polysaccharides. Part III.* Polysaccharide from* Hypnea specifera.

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A polysaccharide was isolated from *Hypnea specifera*, which was precipitated from aqueous solution by potassium chloride and yielded D-galactose and 3 : 6-anhydro-D-galactose and sulphate on hydrolysis. Partial methanolysis followed by hydrolysis and reduction afforded 3 : 6-anhydro-4-*O*-β-D-galactopyranosyl-D-galactitol. Methylation indicated that the galactose was joined to other residues through positions 1 and 3 with the sulphate probably on $C_{(4)}$. It appears to be very similar to κ-carrageenin.

Hypnea specifera is one of the most widely distributed seaweeds of the South African coastline but is of greater importance ecologically in warmer waters. It is believed to be of potential economic importance.[1]

Extraction of fresh, wet *Hypnea specifera* with hot water, followed by filtration and precipitation by ethanol, afforded a crude sulphated polysaccharide in 16% yield (dry weight). This polysaccharide was precipitated by potassium chloride (cf. Smith *et al.*[3]). The material remaining in solution was chiefly protein associated with an insignificant amount of polysaccharide. Polysaccharide, fractionated in this way, was completely converted into the sodium form by suitable ion-exchange resins, precipitated in ethanol, washed, dried, and used as the analytical sample. It had a specific rotation of +66·5° and contained 21·2% of sulphate (calc. as $NaSO_3^-$ on a protein-free basis). Chromatography of the hydrolysate of the polysaccharide showed galactose, a trace of xylose, and a pronounced streak indicating the probable presence of anhydro-sugar.

The galactose was isolated and identified in the usual way by comparison with an authentic specimen. The anhydro-sugar was isolated as its dimethyl acetal by chromatography from the methanolysis products of the polysaccharide, and it was characterised as 3 : 6-anhydro-D-galactose by conversion into the *iso*propylidene derivative of the free

* Part II, *J.*, 1957, 1094.

[1] Isaac and Hewitt, *J. S. African Botany*, 1953, **19**, 73; Fox and Stephens, *S. African J. Sci.*, 1943, **39**, 147.

[2] O'Neill, *J. Amer. Chem. Soc.*, 1955, **77**, 6324.

[3] Smith and Cook, *Arch. Biochem. Biophys.*, 1953, **45**, 232; Smith, Cook, and Neal, *ibid.*, 1954, **53**, 192; Smith, O'Neill, and Perlin, *Canad. J. Chem.*, 1955, **33**, 1353.

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sugar. The yield of galactose was estimated by the Somogyi micro-method,[4] after hydrolysis and separation by paper chromatography,[5] and found to be 47·4% (calc. as $C_6H_{10}O_5$). The content of 3 : 6-anhydro-D-galactose (calc. as $C_6H_8O_4$) was 31·4% by difference. The molecular ratio of galactose : 3 : 6-anhydrogalactose : $NaSO_3$ is thus 1·4 : 1·1 : 1·0.

Partial methanolysis of the polysaccharide and fractionation of the products on cellulose yielded 3 : 6-anhydro-D-galactose dimethyl acetal, a mixture of methyl galactosides, and an amorphous disaccharide dimethyl acetal. The last material failed to crystallise, as did its acetate, and it was hydrolysed with dilute oxalic acid to the free disaccharide, which streaked on paper chromatograms similarly to agarobiose.[6] This sugar was reduced with sodium borohydride, and the product fractionated on cellulose, to yield a crystalline disaccharide glycitol, m. p. 174°, $[\alpha]_D$ +15°. It depressed the m. p. of the agar disaccharide glycitol,[6] m. p. 174°, $[\alpha]_D$ −15°. Hydrolysis of the compound and separation of the products on cellulose afforded D-galactose and a syrup chromatographically identical with 1 : 4-anhydro-L-galactitol (= 3 : 6-anhydro-D-galactitol). The compound formed a crystalline hepta-*O*-acetate. During periodate oxidation 3 mol. of periodate were consumed and 1 mol. of formic acid and 1 mol. of formaldehyde were produced. These facts are consistent with the structure 3 : 6-anhydro-4-*O*-β-D-galactopyranosyl-D-galactitol. The β-configuration was assigned because of the low specific rotation of the compound and its acetate as well as its upward mutarotation on acid hydrolysis. The infrared spectrum of this disaccharide glycitol and of agar disaccharide glycitol[6] displayed the presence of type 2b absorption[7] (bands at 887 and 890 $cm.^{-1}$ respectively for the two compounds) and the absence of type 2a absorption (bands at 844 ± 8 $cm.^{-1}$). This is strong evidence for the presence of a β-glycosidic link.[7] The 1→5 glycosidic linkage was eliminated on stereochemical grounds[8] and the 1→2 linkage would not yield formaldehyde on periodate oxidation.

Methylation of the polysaccharide proved difficult, probably owing to the presence of sulphate groups[9] in the molecule. The final product still contained sulphate (18·3%). Hydrolysis of this product and fractionation of the mixture on cellulose yielded 2 : 6-di-*O*-methyl-D-galactose as the main product. Very small amounts of mono-, tri-, and tetra-*O*-methylgalactose were detected on paper. The methylated anhydrogalactoses were, of course, destroyed by the hydrolysis. The retention of sulphate during methylation suggests that it is not attached to position 3 of the D-galactose residue, as it would easily have been removed by alkaline hydrolysis.[8]

In another experiment the polysaccharide, after methylation with methyl sulphate, was partially hydrolysed with methanolic hydrogen chloride. The resultant mixture was then fully methylated with Purdie's reagents and hydrolysed. Separation of the products on cellulose afforded tetra-*O*-methyl-D-galactose, 2 : 4 : 6-tri-*O*-methyl-D-galactose and 2 : 6-di-*O*-methyl-D-galactose.

The precipitation of the polysaccharide by potassium chloride and the isolation of a disaccharide in high yield seem to indicate that a single polysaccharide is involved. The high yield of disaccharide also indicates that the molecule is largely built up of this unit. Since it seems unlikely that much of the sulphate is attached to position 3 of the galactose,[8] the isolation of 2 : 4 : 6-tri-*O*-methyl-D-galactose after methylation and hydrolysis of partially degraded methylated material, and of 2 : 6-di-*O*-methyl-D-galactose from the hydrolysis of fully methylated material, shows that the galactose is chiefly linked through positions 1 and 3 with half ester sulphate on $C_{(4)}$. Evidence from the structure of the disaccharide glycitol shows that galactose is linked to 3 : 6-anhydro-D-galactopyranose by

[4] Somogyi, *J. Biol. Chem.*, 1952, **195**, 19.
[5] Flood, Hirst, and Jones, *J.*, 1948, 1679.
[6] Clingman, Nunn, and Stephen, *J.*, 1957, 197.
[7] Barker, Bourne, Stacey, and Whiffen, *J.*, 1954, 171, 3468.
[8] Peat, *Adv. Carbohydrate Chem.*, 1946, **2**, 38.
[9] Foster and Huggard, *Adv. Carbohydrate Chem.*, 1955, **10**, 356.

a 1→4 link. Although it is impossible to be certain, it appears that the molecule is mainly linear. The difficulties associated with methylation of a sulphated polysaccharide make it impossible to draw any more conclusions at this stage.

κ-Carrageenin [3] from *Chondrus crispus* is precipitated with potassium chloride and gives the same disaccharide on hydrolysis,[2] and appears to be very similar to *Hypnea* polysaccharide. Araki and Hirase [10] have also isolated this disaccharide from *Chondrus ocellatus*, Holmes.

Experimental

Concentration of solutions was carried out at 40°/20 mm., and specific rotations were measured for aqueous solution unless otherwise stated. Paper chromatograms (Whatman No. 1 paper) were run in (*a*) butanol–ethanol–water (40 : 11 : 19) or (*b*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4). *p*-Anisidine hydrochloride spray was used to detect reducing sugars and a periodate–starch spray [11] to detect non-reducing carbohydrates.

Extraction of the Polysaccharide.—Fresh, wet *Hypnea specifera*, collected near Gordons Bay, Cape, was suspended in water and brought to pH 4 with acetic acid, and steam was passed in for 1 hr. The hot solution, after filtration through a cotton cloth, was centrifuged twice and then poured into ethanol (5 vol.) to precipitate the polysaccharide, which was filtered off, washed with ethanol, acetone, and ether, and dried in a vacuum-desiccator. In another experiment oven-dried seaweed (50 g.) was extracted as described above, to give 8 g. polysaccharide.

An analytical specimen of the polysaccharide was prepared by fractionation with potassium chloride as follows: M-Potassium chloride was added dropwise to a stirred solution of the sodium salt of the polysaccharide (1·55 g.) in water (540 c.c.) until the solution was 0·2M with respect to potassium chloride. The precipitate (1·3 g.) was removed by centrifugation and washed several times with 80% ethanol, twice with absolute ethanol, then with ether, and dried at 60°/20 mm. The material in the supernatant solution was precipitated with alcohol (3 vols.), centrifuged, washed as above, and dried at 60°/20 mm. (0·17 g.) (Found: ash, 40·9; N, 1·4%). It was not further investigated.

The potassium chloride-precipitated polysaccharide (1·3 g.) was dissolved in hot water (200 c.c.) and passed through a column (2·4 × 0·15 cm.) of Amberlite IR-120 resin in the sodium form. Ethanol (3 vols.) was added to the eluate to precipitate the polysaccharide, which was separated by centrifugation. After being washed several times with 80% ethanol, absolute ethanol, and ether it was dried at 60°/20 mm. for 2 days to give a product (1·0 g.), $[\alpha]_D^{17}$ +66·5° (*c* 0·3 in H_2O) (Found: $NaSO_3^-$, 20·4; N, 0·6%).

Isolation and Estimation of D-*Galactose.*—The polysaccharide (1 g.) was hydrolysed with N-sulphuric acid at 100° for 16 hr., and spotted on Whatman No. 3 MM papers which were developed overnight in solvent (*b*). The portions of the papers containing galactose were cut out and extracted (Soxhlet) with methanol. The methanolic solution was concentrated, to give a crystalline product which, after one recrystallisation from methanol, had m. p. and mixed m. p. 166·5—167·5° (with D-galactose), $[\alpha]_D^{18}$ +86° (*c* 1·0).

The polysaccharide was hydrolysed with N-sulphuric acid at 100° for 24 hr. A known amount of maltose was added to the hydrolysate [12] which was neutralised with barium carbonate and chromatographed on paper in solvent (*b*). The strips containing galactose and maltose were cut out and macerated in water; after filtration the sugars were estimated by the Somogyi micro-method [4] [Found: galactose (calc. as $C_6H_{10}O_5$), 47·4% on a moisture-free and protein-free basis].

Methanolysis.—The polysaccharide (21 g.) was refluxed with 2% methanolic hydrogen chloride (210 c.c.) for 20 min. and the mixture was filtered. The insoluble residue (17 g.) was again refluxed in 2% methanolic hydrogen chloride (170 c.c.) for 20 min., and the mixture was filtered. This process was repeated another four times. The filtrates were neutralised with silver carbonate, combined, and concentrated to a syrup (10·2 g.).

Paper chromatograms run in solvent (*a*) disclosed spots of R_R (relative to rhamnose) 0·79, 1·3, and 1·7. The syrup (10 g.) was fractionated on a cellulose column (33 × 5 cm.) with butanol–water (9 : 1). The fractions were sorted by paper chromatography, and like ones combined and concentrated. The first fraction, a syrup (0·96 g.), was chromatographically

[10] Araki and Hirase, *Bull. Chem. Soc. Japan*, 1956, **29**, 770.
[11] Metzenberg and Mitchell, *J. Amer. Chem. Soc.*, 1954, **76**, 4187.
[12] Hough, Jones, and Wadman, *J.*, 1949, 2511.

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identical with 3 : 6-anhydro-D-galactose dimethyl acetal, R_R 1·7 in solvent (*a*), $[\alpha]_D^{17}$ +29° (*c* 1·0), $[\alpha]_D^{17}$ +33° (*c* 1·1 in MeOH): Haworth, Jackson, and Smith [13] report $[\alpha]_D^{18}$ +36·5° (*c* 0·9) for 3 : 6-anhydro-D-galactose dimethyl acetal. It gave a positive Selivanoff reaction.

The syrup (0·8 g.) was hydrolysed in 0·1N-sulphuric acid at 20° for 2 days, neutralised with barium carbonate, and concentrated to dryness. The residue was shaken with acetone (50 c.c.) containing concentrated sulphuric acid (2 c.c.) and anhydrous copper sulphate (5 g.) for 5 hr. The mixture was neutralised with anhydrous potassium carbonate, filtered, boiled with charcoal, and filtered again. The filtrate was concentrated to dryness. The residue in water was extracted with ether. Evaporation of the ethereal solution afforded a solid which, crystallised from light petroleum (b. p. 60—80°), had m. p. and mixed m. p. 90—91° with 1 : 2-*O*-*iso*propylidene-3 : 6-anhydro-D-galactose, $[\alpha]_D^{18}$ +20° (*c* 1·0 in $CHCl_3$) (Araki and Arai [14] report m. p. 92°) (Found: C, 53·4; H, 7·15. Calc. for $C_9H_{14}O_5$: C, 53·5; H, 7·0%).

The next fraction (0·14 g.) off the column, R_R 1·3 in solvent (*a*), probably methyl galactofuranoside, was not investigated.

This was followed by an amorphous substance (3·88 g.), $[\alpha]_D^{16}$ +20° (*c* 1·1); it did not reduce Fehling's solution and gave a positive Selivanoff test. It showed up on paper chromatograms sprayed with *p*-anisidine hydrochloride and heated in an oven (110°) for 15 min. as a yellow spot with the same R_R 0·80 as agarobiose dimethyl acetal. The acetate prepared in the usual way with acetic anhydride and pyridine failed to crystallise. Hence the material (2·8 g.) was hydrolysed in 0·01N-oxalic acid (100 c.c.) at 100° for 3 hr., $[\alpha]_D^{18}$ +20° ⟶ +27° (constant value). The solution was neutralised (Amberlite IR-4B resin) and concentrated to dryness. The residue [long streaky spot of R_R 0·44 in solvent (*a*)] in methanol (100 c.c.) was treated with sodium borohydride (0·35 g.) in methanol (3·5 c.c.) and left overnight. The solution was neutralised (Amberlite IR-120) and concentrated to dryness. The residue was eluted from a cellulose column (27·5 × 3·0 cm.) with butanol–formic acid–water (45 : 1 : 4). The main fraction (2·1 g.), R_R 0·51 in solvent (*a*), was collected and concentrated. A small amount of dulcitol was also obtained, m. p. 188°.

Disaccharide Glycitol.—This substance, crystallised from methanol, had m. p. 173—174°, mixed m. p. with agar disaccharide glycitol [6] (of m. p. 173—174°) 161—163°, $[\alpha]_D^{21}$ +15° (*c* 1·0) (Found: C, 44·2; H, 7·4. Calc. for $C_{12}H_{22}O_{10}$: C, 44·2; H, 6·8%).

Disaccharide glycitol (0·326 g.), in 2N-sulphuric acid (25 c.c.) at 100° for 24 hr., had $[\alpha]_D^{20}$ +14 ⟶ +45·5° (constant value), the final value corresponding to the specific rotation of an equimolar mixture of D-galactose and 1 : 4-anhydro-L-galactitol (= 3 : 6-anhydro-D-galactitol). The hydrolysate was neutralised with barium carbonate and concentrated. Chromatography on papers in solvent (*a*) disclosed two spots having R_{Ga} 1·0 and 2·2 (relative to galactose). The mixture was separated by chromatography on large sheets of paper in the usual way. The one fraction afforded D-galactose (0·080 g., 44·4%), having m. p. and mixed m. p. 166—167° and $[\alpha]_D^{22}$ +82° (*c* 0·8 in H_2O) after crystallisation from methanol. The aglycone was a syrup, (0·077 g., 47·0%), $[\alpha]_D^{22}$ +12° (*c* 1·0), identical with 1 : 4-anhydro-L-galactitol on paper chromatograms. Hockett, Conley, Yusem, and Mason [15] report $[\alpha]_D$ +16·1° for 1 : 4-anhydro-L-galactitol. The disaccharide glycitol (0·1524 g.) was hydrolysed as above and the galactose estimated by the Somogyi micro-method,[4] maltose being used as a standard [12] (Found: 1·11, 1·04 mol. of galactose per mol. of disaccharide glycitol).

Disaccharide glycitol (0·3 g.) in pyridine (5 c.c.) was treated with acetic anhydride (5 c.c.) in pyridine (3 c.c.) at 5°. After 2 days at 5° and 2 days at room temperature the mixture was poured into ice-water (200 c.c.) with stirring. The acetate was filtered off and recrystallised from 96% ethanol; it had m. p. 144—145°, $[\alpha]_D^{22}$ −7·6° (*c* 1·05 in $CHCl_3$) (Found: C, 50·8; H, 6·4; Ac, 49·9. Calc. for $C_{26}H_{36}O_{17}$: C, 50·3; H, 5·9; Ac, 48·5%).

Periodate Oxidation of Disaccharide Glycitol.—To the disaccharide glycitol (0·1234 g.) in water (25 c.c.) was added 0·4M-sodium metaperiodate (5·0 c.c.), and the solution made up to 50 c.c. The progress of the reaction, which was complete in 24 hr. was followed by titration (0·01N-sodium hydroxide) of aliquot parts at regular intervals (Bromocresol Purple) [16] after destruction of excess of periodate with ethylene glycol. The periodate consumed was then determined in the usual way, and the formaldehyde was estimated on an aliquot portion as its

[13] Haworth, Jackson, and Smith, *J.*, 1940, 620.
[14] Araki and Arai, *J. Chem. Soc. Japan*, 1942, **63**, 1720; *Chem. Abs.*, 1947, **41**, 3765.
[15] Hockett, Conley, Yusem, and Mason, *J. Amer. Chem. Soc.*, 1946, **68**, 922.
[16] Hartman, *J. Appl. Chem.*, 1953, **3**, 308.

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dimedone derivative,[17] m. p. and mixed m. p. 188—189° (Found: 0·95 mol. of formic acid, 0·75 mol. of formaldehyde produced, and 2·98 mol. of periodate consumed).

Methylated Polysaccharide.—The polysaccharide (15 g.) in hot water (150 c.c.) was treated with methyl sulphate (225 c.c.), and 30% sodium hydroxide solution (675 c.c.) was added during 7 hr. A little acetone was added to the mixture during methylation to help dissolve the methylated material. The mixture was heated at 80° for 30 min. and then neutralised with 50% sulphuric acid. The solution was filtered free from precipitated sodium sulphate, concentrated, and freed from more sodium sulphate by the addition of 60% ethanol. The methylation and concentration procedure was repeated three times.

The final product, in water, was dialysed against running tap-water for 10 days, then concentrated to a residue (2 g.). Those sodium sulphate precipitates which gave a positive Molisch test were also dissolved in water and dialysed against running tap-water for 10 days. The dialysate was concentrated to give a product (0·8 g.) which was combined with the main batch of methylated material (Found: OMe, 20·9; SO_4^{2-}, 18·3%).

The methylated polysaccharide (2·3 g.) in N-sulphuric acid (23 c.c.) was hydrolysed at 100° for 20 hr., neutralised with barium carbonate, and concentrated to a syrup (1·34 g.). Chromatography on paper in solvent (*a*) revealed the presence of 2 : 6-di-*O*-methylgalactose, R_{TMG} (relative to tetramethylglucose) 0·64, together with small amounts of mono-*O*-methylgalactose, R_{TMG} 0·41, tri-*O*-methylgalactose, R_{TMG} 0·77, and tetra-*O*-methylgalactose, R_{TMG} 0·90, and also a furfuraldehyde derivative just behind the solvent front. The syrup (1·3 g.) on a cellulose column (35 × 3·5 cm.) irrigated with butanol–water (9 : 1) yielded as main fraction a syrup (0·7 g.), R_{TMG} 0·64. This syrup crystallised from ethyl acetate, then having m. p. and mixed m. p. 128·5—130° with synthetic [18] 2 : 6-di-*O*-methyl-D-galactose, $[\alpha]_D$ +45° ⟶ +88° (*c* 0·8) (Found: C, 46·4; H, 7·9; OMe, 28·9. Calc. for $C_8H_{16}O_6$: C, 46·2; H, 7·75; OMe, 29·8%).

Methylation of Partially Degraded Methylated Polysaccharide.—The polysaccharide (11 g.) in water (70 c.c.) was methylated with methyl sulphate (150 c.c.) and 30% sodium hydroxide solution (450 c.c.) in the usual way. The reaction mixture was freed from excess of sodium sulphate, and the methylation procedure repeated a further six times. The final solution was dialysed against running water and concentrated, to yield a residue (6·6 g.) (Found: OMe, 21·4; SO_4^{2-}, 16·0%). This residue (6·2 g.) was shaken at 30° for 16 hr. with 1% methanolic hydrogen chloride (300 c.c.). After centrifugation to remove a trace of undissolved material, the clear solution was neutralised with silver carbonate and concentrated to a syrup (5·4 g.) (Found: OMe, 32·0; SO_4^{2-}, 7·7%). The syrup (5·0 g.) in dry methanol (10 c.c.) was twice methylated according to Purdie's method [19] with Drierite (1 g.), methyl iodide (30 c.c.), and silver oxide (30 g.) each time, to yield a syrup (3·4 g.), $[\alpha]_D^{28}$ +7° (*c* 1·2) (Found: OMe, 35·8; SO_4^{2-}, 7·4%).

The syrup (2·9 g.) was hydrolysed in N-sulphuric acid at 95° for 16 hr. and the solution neutralised with barium carbonate and concentrated to a syrup (2·1 g.). The latter was fractionated on a cellulose column (35 × 3·5 cm.) with butanol–light petroleum [12] (b. p. 100—120°) (2 : 3) to yield two fractions.

Fraction I (0·4 g.), a syrup, identical with tetra-*O*-methylgalactose on chromatograms, was treated with aniline to yield a derivative, m. p. and mixed m. p. 189—190° with 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-galactosylamine.

Fraction II (0·35 g.), a syrup, was a mixture of tri- and tetra-*O*-methylgalactose (paper chromatograms). These were resolved by chromatography on large sheets of paper (Whatman No. 20) in solvent (*a*). The tri-*O*-methylgalactose fraction (0·2 g.) was heated with aniline in the usual way, to yield a product, m. p. 170·5—171·5° after recrystallisation from ethanol, $[\alpha]_D^{20}$ −80° ⟶ +38·2° (*c* 1·1 in acetone). Hirst and Jones [20] reported m. p. 179° (sometimes 169°), $[\alpha]_D$ −92° ⟶ +38° (in acetone), for 2 : 4 : 6-tri-*O*-methyl-*N*-phenyl-D-galactosylamine. None of this was available for comparison, but our specimen depressed the m. p. of 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-galactosylamine (m. p. 163—164°) supplied by Dr. A. M. Stephen.

After fraction II had been removed the column was eluted with ethanol, the solution concentrated, and the resulting syrup resolved on a large paper chromatogram in solvent (*a*). Apart from some further tri-*O*-methyl-D-galactose this yielded 2 : 6-di-*O*-methyl-D-galactose

[17] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1477.
[18] Bell, *J.*, 1945, 692.
[19] Purdie and Irvine, *J.*, 1903, 1021.
[20] Hirst and Jones, *J.*, 1939, 1482.

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(0·09 g.) which, crystallised from ethyl acetate, had m. p. and mixed m. p. 128·5—130°. A very small quantity of a mono-*O*-methylgalactose, R_{TMG} 0·36, was also obtained.

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NATIONAL CHEMICAL RESEARCH LABORATORY,
PRETORIA, SOUTH AFRICA. [*Received, October 7th,* 1958.]

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103. *Rare-earth Carbides. Part I.*

By R. C. VICKERY, R. SEDLACEK, and ARDYS RUBEN.

Higher carbides of some rare earths have been prepared by reaction of rare-earth oxides and carbon at high temperatures under low pressures of argon. Formation of carbide proceeds *via* the metal, and interstitial compounds can exist of rare-earth metal held in the carbide lattice.

The higher carbides (LnC_2) adopt a tetragonal structure, but scandium differs from the lanthanons and yttrium in forming only a hexagonal monocarbide (ScC); this is attributed to the small size of the scandium ion which permits its association with only one carbon atom.

THE rare-earth elements are generally accepted as forming " salt-like " carbides containing C_2^{2-} ions in their lattices.[1] This concept of an Ln(C≡C) structure is of interest because it represents the compounds as acetylide salts of bivalent elements, even for lanthanum, cerium, terbium, gadolinium, etc., which do not otherwise show indications of potential bivalency.[2] The problem is more formidable since Warf [3] and Spedding and his co-workers [4] showed that two rare-earth carbide phases exist. Warf suggests that these are LnC and LnC_3, LnC_2 being considered a mixture of these, but Spedding's group have identified both LaC_2 and La_2C_3 entities. We have confirmed the existence of two rare-earth carbide phases, LnC_2 and a lower carbide not yet completely identified.

Stackelberg [5] and Spedding *et al.*[4] attempted to explain the incongruity of the LnC_2 molecule by assuming that, of the three valency electrons in a rare-earth ion, only two are effective in carbide formation, the third (probably 5*d*) remaining " free " in a conduction band and being responsible for the metallic nature and electrical conductivity of the carbides. If this be so, then magnetic susceptibilities and *X*-ray spectra of the carbides should disclose this " free " electron; these aspects are reported in the following papers. The present paper reports synthesis of the higher carbides by reaction of rare-earth oxides and carbon, and studies on their primary reactions and crystallography.

Stackelberg's *X*-ray studies [5] indicated that the carbides (LnC_2) adopt a face-centred tetragonal structure, which Wells [1] interprets as a calcium carbide variation of the rock-salt lattice, the chloride ions being replaced by acetylide ions, thus lowering the symmetry to tetragonal with an axial ratio greater than unity. Spedding *et al.*[4] found their lower lanthanum carbide (La_2C_3) to be body-centred cubic ($a = 8·817$) and their higher carbide (LaC_2) to be body-centred tetragonal ($a = 3·934$, $c = 6·572$); Warf [3] found his monocarbides to be isostructurally hexagonal, the CeC unit cell having $a = 6·84$, $c = 12·77$, $c/a = 1·87$. The tricarbides were stated to be face-centred tetragonal, CeC_3 having $a = 5·49$, $c = 6·51$, $c/a = 1·19$. We find the dicarbides to be tetragonal, and the powder

[1] Sidgwick, " Chemical Elements and Their Compounds," Vol. 1, p. 440, Oxford Univ. Press, 1950; Wells, " Structural Inorganic Chemistry," p. 457, Oxford Univ., Press, 1945; Huckel, " Structural Chemistry of Inorganic Compounds," Vol. II, p. 887, Elsevier, 1951.

[2] Yost, Russell, and Garner, " Rare Earth Elements and Their Compounds," p. 4, Wiley, 1947; Vickery, " Chemistry of the Lanthanons," p. 57, Butterworths, 1953.

[3] Warf and Palineck, Status Report, July 20, 1955, U.S. Office of Ordnance Research, Project 683, Contract DA-04-495-Ord, 1955/6.

[4] Spedding and Daane, USAEC–ISC 757, 1956; Atoji, Gschneidner, Daane, Rundle, and Spedding, *J. Amer. Chem. Soc.*, 1958, **80**, 1804.

[5] von Stackelberg, *Z. phys. Chem.*, 1930, *B*, **9**, 437.

diffraction patterns indexable as either body- or face-centred structures. In the absence of single-crystal studies it is convenient to assume a structure based upon the smallest cell size possible, in this case the body-centred cell which contains two formula units per unit cell as compared with the four formula units indicated by a face-centred tetragonal habit. The values obtained in this work for crystal lattice constants, etc., are given in Table 1 wherein are indicated the lattice parameters applicable to both types of structure.

Stackelberg [5] and Gaume-Mahn [6] considered yttrium carbide to differ from the lanthanon carbides in adopting a hexagonal habit, but we found no evidence for it. However, from scandium carbide, by our procedure, we have been able to prepare only the monocarbide of hexagonal habit with cell parameters as indicated in Table 1, the unit cell containing ten formula units. Otherwise, the structures and parameters now found for the dicarbides confirm those of Stackelberg and Spedding's groups, but we must emphasise that our lattice data were formulated from powder-diffraction patterns. As Hunt and Rundle [7] demonstrated for thorium carbide, single-crystal studies are nesessary for full structural evaluation; we have been unable to produce the necessary carbide single crystals.

There is evidence that rare-earth carbides are produced by interaction of the oxide and carbon *via* the metal. This appears to be the first time that this reduction has been observed; whether the lower carbide forms as a secondary or intermediate product has yet to be determined. However, the rare-earth carbides can form compounds with interstitial rare-earth metal atoms. When heated *in vacuo*, this interstitial metal volatilises leaving LnC_2.

TABLE 1. *Parameters of higher rare-earth carbides.*

Element	Element (%) Found	Calc.	C/Ln	D_o	D_T	Struct.	a_o	c_o	c/a	Molecules/ unit cell
Sc	78·0	78·9	1	3·60	3·59	hex.	5·46	10·24	1·88	10
Y	72·9	71·2	2	4·78	4·53	b.c.t.	3·66	6·17	1·68	2
					4·55	f.c.t.	5·17	6·17	1·19	4
La.....	84·6	85·3	2	5·29	5·36	b.c.t.	3·92	6·57	1·68	2
					5·36	f.c.t.	5·54	6·57	1·19	4
Ce	84·8	84·8	2	5·56	5·58	b.c.t.	3·88	6·49	1·67	2
					5·57	f.c.t.	5·49	6·49	1·18	4
Pr	86·7	85·5	2	5·58	5·72	b.c.t.	3·86	6·44	1·67	2
					5·73	f.c.t.	5·45	6·44	1·18	4
Nd	85·7	85·7	2	5·93	5·98	b.c.t.	3·83	6·40	1·67	2
					5·98	f.c.t.	5·41	6·39	1·18	4
Sm	86·3	86·2	2	6·42	6·48	b.c.t.	3·76	6·31	1·68	2
					6·47	f.c.t.	5·32	6·33	1·19	4
Gd	87·2	86·7	2	6·93	6·93	b.c.t.	3·72	6·27	1·69	2
					6·92	f.c.t.	5·25	6·27	1·19	4
Tb	86·6	86·9	2	7·09	7·19	b.c.t.	3·69	6·21	1·68	2
					7·20	f.c.t.	5·22	6·21	1·19	4
Dy	86·7	87·3	2	7·38	7·59	b.c.t.	3·64	6·15	1·69	2
					7·59	f.c.t.	5·15	6·15	1·19	4
Ho	87·5	87·4	2	7·76	7·83	b.c.t.	3·62	6·11	1·69	2
					7·83	f.c.t.	5·13	6·11	1·19	4
Er	86·8	87·5	2	7·70	7·96	b.c.t.	3·61	6·11	1·69	2
					7·97	f.c.t.	5·11	6·11	1·20	4
Yb	86·9	87·8	2	7·97	8·20	b.c.t.	3·62	6·09	1·68	2
					8·20	f.c.t.	5·12	6·09	1·19	4

Understanding of the Ln–C bond from present data is difficult. There is now little doubt that the highest carbide of yttrium and the lanthanons is the dicarbide. This work confirms the appropriate area of Spedding and his co-workers' phase diagram, and Chupka *et al.*[8] indicate that the dicarbide is thermodynamically the most stable compound: there is thus little support for Warf's LaC_3 structure, which was probably LaC_2 plus excess of carbon.

Although the higher electron affinity of the $(C{\equiv}C)^{2-}$ entity favours formation of the

[6] Gaume-Mahn, *Bull. Soc. chim. France*, 1956, 1862.
[7] Hunt and Rundle, *J. Amer. Chem. Soc.*, 1951, **73**, 4777.
[8] Chupka, Berkowitz, Giese, and Inghram, *J. Phys. Chem.*, 1958, **62**, 611.

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dicarbide, there must be a limiting radius for the cation to which such a strongly directional anion can be attached. From the formation of ScC, this limit appears to lie between 0·8 and 1·00 Å. We might expect a tendency, through the lanthanide contraction, for the formation of carbides variant from LnC_2, but this is not apparent. The fact that YC_2 parameters come before those of DyC_2 instead of after is considered to indicate the development of covalency as one proceeds towards the heavier and smaller lanthanons, and this might well suffice to compensate for the strain introduced by the decreasing atomic radii. To some extent this is substantiated by sesquicarbides' (analogous in concept to Ln_2O_3) not having been observed [4] in rare earths of ionic radius less than that of holmium. On the other hand, if the C_2^{2-} unit behaves similarly to an oxygen atom, as suggested by Chupka *et al.*, the formation of ScC as a stable entity seems to be inconsistent with the stable ScO predicted by them.

It is significant that hexagonal ScC is isostructural with Warf's monocarbides and with scandium metal, which suggests some similarity to Hägg's interstitial structure.[9] It is of interest to compare scandium carbide and nitride. The latter (ScN) is face-centred cubic and is very inert chemically; nitrides of the other rare earths are also cubic (at least as far as gadolinium) but less resistant to reagents.[6] It is generally accepted that hard, high-melting carbides of the type MX adopt a cubic NaCl type of structure, but scandium carbide is anomalous, particularly since the radius ratio of 0·48 for ScC is adequately close

TABLE 2. *Comparison of melting points.*

	1	2	3	4		1	2	3	4
La.....	1600°	2000°	600°	>2000°	Sm	1700°	2000°	1100°	>2200°
Ce	1600	>2000	620	>2300	Gd	1700	>2000	1000	>2200
Pr	1650	1900	750	>2200	Y	1950	>2000	1250	>2300
Nd	1650	1900	650	>2000					

1, Temp. of carbide formation; 2, m. p. of oxide; 3, m. p. of metal; 4, m. p. of carbide (all at 10 mm. Hg).

TABLE 3. *Ratios of radii and composition of some Group III carbides.*

Element	Metal radius, Å	Radius ratio,* C/Me	Carbide	Composition ratio, C/Me
B	0·87	0·76	B_4C	0·25
Al	1·43	0·47	Al_4C_3	0·75
Sc	1·60	0·42	ScC	1·00
Y	1·80	0·37	YC_2	2·00
La	1·87	0·36	LaC_2	2·00
Yb	1·93	0·34	YbC_2	2·00

* Radius of C = 0·665 Å.

to the value 0·41 theoretically required for an exact fit in the NaCl structure. However, as Hume-Rothery [10] points out, the close-packed hexagonal structure contains one " octahedral interstice " per metal atom, which permits the same anion environment for the anion in MX as does the cubic structure. Our preparation of hexagonal scandium monocarbide, and considerations on the serial position of yttrium carbide, agree with Hume-Rothery's thesis that covalency is necessary in these compounds. Again, in comparison, the weaker, triply bonded nitrogen atoms clearly require a crystal structure of lower symmetry than do those with quadrivalent carbon.*

A further aspect of the radius-ratio effect and covalency in carbides can be developed by comparing the ratios and compositions for Group III carbides (Table 3). Spedding *et al.*[4] have shown that the C–C bond distance in LaC_2 is intermediate between that of a

* No data appear to be available on scandium phosphide or silicide, but from the above it would seem logical to expect hexagonal structures for these compounds.

[9] Hägg, *Z. phys. Chem.*, 1929, *B*, **6**, 221; 1931, *B*, **12**, 33.
[10] Hume-Rothery, *Phil. Mag.*, 1953, **44**, 1154.

double and a triple bond, whilst in the sesquicarbide the distance is that of a double bond. A simple construction could therefore be presented which, whilst accounting for the LnC_2 structure, does not require the concept of a " free " electron. In a unit cell with two formula-units, the six valency electrons of the two La atoms are allocated between one triple-bonded and one double-bonded C_2 unit. Such a system would adequately account for the mixture of hydrocarbons evolved on hydrolysis, but seems invalidated by the apparent conductivity of the carbides.

In the ScC structure, with 10 units per unit cell, the construction of a hexagon from $(C–C)^{6-}$ bonds is simple; such a structure can well be expected to have the resistance to hydrolysis and acid shown by this monocarbide.

We have also considered the possibility that, since an oxide is reduced to metal during formation of the carbides, bivalent samarium and ytterbium might also be produced. Our magnetochemical work on the carbides develops this theme and now we are concerned with the structures which might be developed around Sm^{2+} and Yb^{2+}. Such bivalent lanthanons could be assumed to associate with the $[C{\equiv}C]^{2-}$ without requiring a free-electron. The bivalent ions would, however, be larger than the tervalent form, and this should be reflected in the size of the crystal lattice. Comparison of the lattice parameters of SmC_2 with those of the neodymium compound shows, however, only the average difference between neighbours (interpolation of promethium being allowed for). The lattice parameters of ytterbium carbide are, however, identical with those of erbium carbide, which might be attributable to ytterbium's becoming bivalent, with correspondingly larger atomic radius.

Experimental

Previous work contains few details of synthesis of rare-earth carbides. Spedding's group [4] prepared their carbides by reaction of rare-earth metal and carbon in the electric arc but apparently did not investigate the Ln_2O_3–C systems. Moissan [11] heated rare-earth oxides and carbon in an electric arc furnace but gave no details. de Villélume [12] reduced La_2O_3 by carbon at 2000° c in nitrogen or hydrogen, carbide formation in the former instance being preceded by that of nitrides. He reported that CeC_2 was pyrophoric, and that carburisation proceeded rapidly at 1000° c. Gaume-Mahn [6] states that the carbides fuse at 1800—2000° c but gives no indications of the atmosphere or pressure employed. We avoided nitrogen or hydrogen, employing argon instead, and confirmed that CeC_2, alone of the dicarbides, is pyrophoric and that all the dicarbides have m. p.s higher than 1800° c. (In subsidiary work we found no direct carbide formation to occur between rare-earth oxides and carbon below 1600° c in nitrogen.)

The rare-earth oxides and carbon used were more than 99·8% pure, the oxides having been separated from crude sources by ion exchange, and the carbon being " Black G " grade which had been vigorously outgassed at high temperatures. We used two types of furnace—a 5 kv induction furnace for massive carbide formation, and a low-capacity high-temperature resistor furnace operating at up to 300 A to give a crucible temperature of *ca.* 2500° c. Both furnaces could be used under vacuum or with argon.

The general reactions involved in producing the lowest and the highest carbide reported appear to be:

$$2Ln_2O_3 + 7C \longrightarrow 4LnC + 3CO_2$$
$$2Ln_2O_3 + 15C \longrightarrow 4LnC_2 + 3CO_2$$

Varying ratios of Ln_2O_3 : C were employed in preliminary studies but, since the crucible used was of graphite, observation of differential effects was difficult. Molybdenum crucible liners reacted with the oxide–carbon mixture at the temperatures employed, and in some runs at low carbon ratios and low temperatures gave evidence for the formation of increased amounts of a silvery lower carbide, but generally the results were not reproducible. The most definite example of lower carbide production was obtained from a 1 : 5 mole ratio of La_2O_3 : C at 1900° c and 1·5 mm. pressure of argon. The carbide produced was visibly heterogeneous, the gold-coloured high carbide at the crucible–product interface enclosing a central body of silvery, lower carbide. Analyses showed the two phases to be LaC_2 and LaC, respectively.

[11] Moissan, *Compt. rend.*, 1900, **131**, 595.
[12] de Villélume, *Ann. Chim.*, 1952, **7**, 265; *Compt. rend.*, 1951, **231**, 142, 1497; **232**, 235.

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Yb	1·93	0·34	YbC_2	2·00

* Radius of C = 0·665 Å.

to the value 0·41 theoretically required for an exact fit in the NaCl structure. However, as Hume-Rothery [10] points out, the close-packed hexagonal structure contains one " octahedral interstice " per metal atom, which permits the same anion environment for the anion in MX as does the cubic structure. Our preparation of hexagonal scandium monocarbide, and considerations on the serial position of yttrium carbide, agree with Hume-Rothery's thesis that covalency is necessary in these compounds. Again, in comparison, the weaker, triply bonded nitrogen atoms clearly require a crystal structure of lower symmetry than do those with quadrivalent carbon.*

A further aspect of the radius-ratio effect and covalency in carbides can be developed by comparing the ratios and compositions for Group III carbides (Table 3). Spedding *et al.*[4] have shown that the C–C bond distance in LaC_2 is intermediate between that of a

* No data appear to be available on scandium phosphide or silicide, but from the above it would seem logical to expect hexagonal structures for these compounds.

[9] Hägg, *Z. phys. Chem.*, 1929, *B*, **6**, 221; 1931, *B*, **12**, 33.
[10] Hume-Rothery, *Phil. Mag.*, 1953, **44**, 1154.

double and a triple bond, whilst in the sesquicarbide the distance is that of a double bond. A simple construction could therefore be presented which, whilst accounting for the LnC_2 structure, does not require the concept of a " free " electron. In a unit cell with two formula-units, the six valency electrons of the two La atoms are allocated between one triple-bonded and one double-bonded C_2 unit. Such a system would adequately account for the mixture of hydrocarbons evolved on hydrolysis, but seems invalidated by the apparent conductivity of the carbides.

In the ScC structure, with 10 units per unit cell, the construction of a hexagon from $(C-C)^{6-}$ bonds is simple; such a structure can well be expected to have the resistance to hydrolysis and acid shown by this monocarbide.

We have also considered the possibility that, since an oxide is reduced to metal during formation of the carbides, bivalent samarium and ytterbium might also be produced. Our magnetochemical work on the carbides develops this theme and now we are concerned with the structures which might be developed around Sm^{2+} and Yb^{2+}. Such bivalent lanthanons could be assumed to associate with the $[C\equiv C]^{2-}$ without requiring a free-electron. The bivalent ions would, however, be larger than the tervalent form, and this should be reflected in the size of the crystal lattice. Comparison of the lattice parameters of SmC_2 with those of the neodymium compound shows, however, only the average difference between neighbours (interpolation of promethium being allowed for). The lattice parameters of ytterbium carbide are, however, identical with those of erbium carbide, which might be attributable to ytterbium's becoming bivalent, with correspondingly larger atomic radius.

Experimental

Previous work contains few details of synthesis of rare-earth carbides. Spedding's group [4] prepared their carbides by reaction of rare-earth metal and carbon in the electric arc but apparently did not investigate the Ln_2O_3–C systems. Moissan [11] heated rare-earth oxides and carbon in an electric arc furnace but gave no details. de Villélume [12] reduced La_2O_3 by carbon at 2000° c in nitrogen or hydrogen, carbide formation in the former instance being preceded by that of nitrides. He reported that CeC_3 was pyrophoric, and that carburisation proceeded rapidly at 1000° c. Gaume-Mahn [6] states that the carbides fuse at 1800—2000° c but gives no indications of the atmosphere or pressure employed. We avoided nitrogen or hydrogen, employing argon instead, and confirmed that CeC_2, alone of the dicarbides, is pyrophoric and that all the dicarbides have m. p.s higher than 1800° c. (In subsidiary work we found no direct carbide formation to occur between rare-earth oxides and carbon below 1600° c in nitrogen.)

The rare-earth oxides and carbon used were more than 99·8% pure, the oxides having been separated from crude sources by ion exchange, and the carbon being " Black G " grade which had been vigorously outgassed at high temperatures. We used two types of furnace—a 5 kv induction furnace for massive carbide formation, and a low-capacity high-temperature resistor furnace operating at up to 300 A to give a crucible temperature of *ca.* 2500° c. Both furnaces could be used under vacuum or with argon.

The general reactions involved in producing the lowest and the highest carbide reported appear to be:

$$2Ln_2O_3 + 7C \longrightarrow 4LnC + 3CO_2$$
$$2Ln_2O_3 + 15C \longrightarrow 4LnC_2 + 3CO_2$$

Varying ratios of Ln_2O_3 : C were employed in preliminary studies but, since the crucible used was of graphite, observation of differential effects was difficult. Molybdenum crucible liners reacted with the oxide–carbon mixture at the temperatures employed, and in some runs at low carbon ratios and low temperatures gave evidence for the formation of increased amounts of a silvery lower carbide, but generally the results were not reproducible. The most definite example of lower carbide production was obtained from a 1 : 5 mole ratio of La_2O_3 : C at 1900° c and 1·5 mm. pressure of argon. The carbide produced was visibly heterogeneous, the gold-coloured high carbide at the crucible–product interface enclosing a central body of silvery, lower carbide. Analyses showed the two phases to be LaC_2 and LaC, respectively.

[11] Moissan, *Compt. rend.*, 1900, **131**, 595.
[12] de Villélume, *Ann. Chim.*, 1952, **7**, 265; *Compt. rend.*, 1951, **231**, 142, 1497; **232**, 235.

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The appearance of the carbide slugs and their proximity to the crucible wall suggested that liquefaction occurred during reaction. Although CO and CO_2 were always evolved, attempts to obtain a material-balance were spoilt by reaction of the crucible carbon.

Through several preparations the synthetic procedure developed was: appropriate oxide–carbon mixtures were placed in a graphite crucible in a 5 kv induction furnace. The system was thrice evacuated and flushed with pure argon. Finally the temperature was raised to *ca.* 1600° c, with pressure maintained at 15 lb./sq. in. of argon. During the preliminary heating the reactants shrank from the crucible walls, but little if any reaction occurred at 15 lb./sq. in. At 1600° c, vacuum was gradually applied until reaction proceeded steadily, as shown by continuous evolution of gas. The pressure required for such reaction varied slightly with temperature, and for the formation of lanthanum carbide, the pressures at 1600°, 1700°, 1800°, and 1900° were 10, 14, 17, and 20 mm. Hg, respectively.

The observed temperature of reaction at 10 mm. Hg appeared to increase through the series from La to Tb, being highest with yttrium at 1950° c. The rate was controlled by adjusting both temperature and pressure until the reaction had passed through the degassing stage (*a*), followed by a molten stage (*b*), to a reconsolidation stage (*c*). The whole sequence for a charge containing *ca.* 15 g. of Ln_2O_3 was complete in about 3 hr. As soon as stage (*b*) was reached, the temperature was generally increased to *ca.* 2100° to accelerate passage of (*b*) and (*c*) stages.

When cool, the product was a crystalline, yellow button containing excess of carbon, most of which, derived from the crucible, was separated, after crushing, by levigation with anhydrous kerosene or benzene. (Complete absence of water is necessary to avoid hydrolysis.) After removal of gross free carbon, the carbide was washed twice with anhydrous acetone, twice with ether, and then stored in evacuated tubes. Rate of hydrolysis with water, either directly or derived from the atmosphere, increases with decreasing size of the carbide granules, and it was undesirable to reduce this below about 100 mesh.

The carbides were analysed (Table 1) by dissolution in dilute acid, removal of remaining free carbon by filtration, and precipitation of the rare-earth content as oxalate followed by ignition to oxide. Scandium carbide is somewhat refractory to this treatment; it hydrolyses and dissolves in acid much less readily than do the other rare-earth carbides; also, it is greyish-black whereas, for example, LaC_2, GdC_2, and YC_2 are brassy yellow.

X-Ray diffraction patterns were taken on a G.E. XRD powder camera with a radius of 14·32 cm. in Cu-K_α radiation, with a nickel filter, at 50 kv and 16 mA. The exposure time was 5 hr. which gave generally satisfactory results for most carbides. Adequate patterns for samarium and gadolinium carbides were obtained only with Mo-K_α radiation, since the absorption spectra and edges of the carbides differ markedly from those of the corresponding metals or oxides. Data for *X*-ray absorption spectra suggest gross perturbation of the *K* and *L* levels of the rare-earth ions on carbide formation (see Part III).

In general, *X*-ray studies showed the lanthanon and yttrium carbides to be tetragonal; cell constants and derived densities are listed in Table 1, together with densities determined pyknometrically against anhydrous *p*-xylene.

The liquefaction and reconsolidation observed during reaction, coupled with the appearance of carbide ingots, suggested formation of an intermediate of lower m. p. than the final carbide. This could be postulated as due to (*a*) melting of the oxide, (*b*) intermediate formation of a lower carbide of low m. p., or (*c*) intermediate production of metal. Supplementary direct observations in the resistor furnace showed that the final carbide was formed at temperatures below the m. p. of the oxide and that of the higher carbide but above that of the metal (Table 2).

Spedding *et al.*[4] have reported a eutectic in the La–C system, *viz.*, La_4C, melting at *ca.* 840° c; they employed metal as one reactant, however, and we could not obtain this quadricarbide in oxide–carbon systems. Instead, experiments in which Ln_2O_3–C mixtures were quenched just at the liquefaction point showed the presence of reguli, identifiable by *X*-ray and chemical examination as rare-earth metal.

Mixtures of rare-earth metals, and oxides with the carbon required for higher carbide stoicheiometry, yielded, when heated under the conditions given above, a metallic-looking carbide which, on levigation from the mass, was reheated *in vacuo*. A vapour was produced, and the carbide granules crumbled to a fine powder. The vapours condensed in thin films shown by *X*-ray and chemically to be rare-earth metal, on cool molybdenum surfaces. The residual powders were shown similarly to be LnC_2 carbides, whereas chemical examination of the

primary product gave Ln contents higher than required for, *e.g.*, LnC, although *X*-ray patterns showed little difference from the LnC_2 pattern. The rare-earth carbides thus appear somewhat analogous to those of uranium, in which similar interstitial behaviour is observed.

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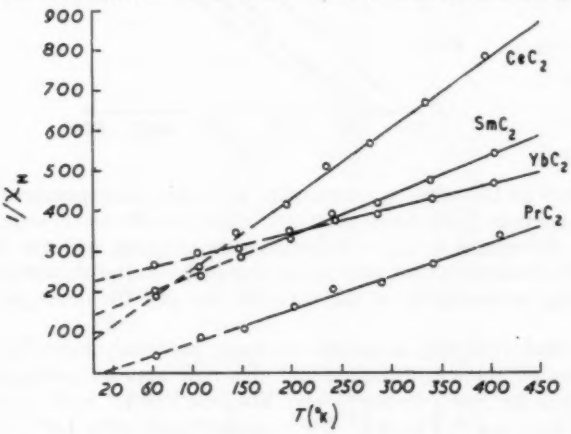
104. *Rare-earth Carbides. Part II.* Magnetochemistry.*

By R. C. VICKERY, R. SEDLACEK, and ARDYS RUBEN.

The intrinsic paramagnetism of tervalent rare-earth ions is affected only slightly by carbide formation. Except for samarium and ytterbium dicarbides, the small negative difference noted between the theoretical and the observed magnetism is attributed to partial spin coupling or quenching of the orbital angular moments. As carbides, samarium and ytterbium are considered to adopt their bivalent states. Bohr magneton numbers and Curie–Weiss constants are presented.

MAGNETIC susceptibilities for rare-earth metals agree[1,2] very well with the free gas susceptibility values of the tervalent ions. Within the limits indicated below, the rare-earth carbides are now found to have magnetic susceptibilities agreeing with those of the

FIG. 1. *Susceptibility of lanthanon dicarbides as a function of absolute temperature.*



free ions and metals. There is some evidence, however, that in samarium and ytterbium dicarbides these lanthanons tend to be bivalent. This confirms to some extent our earlier structural considerations. Europium carbide was not studied.

Magnetochemical studies on carbides have been but little pursued, so data cannot be compared. We have, moreover, had to employ an empirical value of $0{\cdot}3 \times 10^{-6}$ c.g.s.

* Part I, preceding paper.

[1] Rhodes, Legvold, Elliott, Behrendt, and Spedding, USAEC–ISC–378, 1953; *Phys. Rev.*, 1958, **109**, 1544, 1547.

[2] LaBlanchetais, Thesis, Université de Paris, 1954; Selwood, "Magnetochemistry," 2nd edn., Interscience, New York, 1956.

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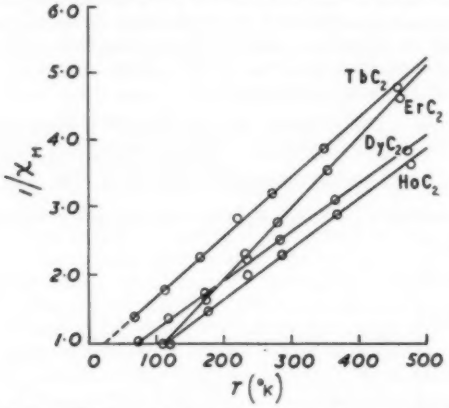
unit for the diamagnetism of the $(C{\equiv}C)^{2-}$ entity based upon comparison of the susceptibilities of C–C and C=C and a tentative application of Slater's method of calculation.[3] The $(C{\equiv}C)^{2-}$ entity has been assumed to be present in the rare-earth carbides (preceding paper and ref. 2); and the fact that, after correction for its empirical value, values of $\mu_{eff.}$ have been obtained for the Ln^{3+} ions, agreeing with standard data, tends to confirm that the rare-earth dicarbides are, in effect, acetylide salts.

Figs. 1 and 2 show values of $1/\chi_M$ plotted against $T°$ K, and the Table shows $\mu_{eff.}$, C, and θ values derived from the graphs through the Curie–Weiss formula, $\mu = 2{\cdot}839\sqrt{[\chi_M(T - \theta)]}$. Negative θ values are of no significance, serving merely to indicate the absence of potential ferromagnetism. Susceptibilities and field strength exhibit a simple horizontal linear relationship, again indicating absence of ferromagnetism. Although gadolinium metal has a ferromagnetic Curie temperature of 16° C,[1] this transition was not observed in the carbide; similarly, we did not observe the reported susceptibility minimum for samarium at 400° K.[4] Temperature–susceptibility curves for dysprosium carbide were not taken to temperatures low enough for observation of the antiferromagnetic anomaly observed in the

FIG. 2. *Susceptibility of lanthanon dicarbides as a function of lanthanon dicarbides.*



metal by Trombe [5] at 150—200° K. Generally, although many points of resemblance to metallic paramagnetism have been observed, there remain some areas of distinction, particularly the differences in $\mu_{eff.}$. Although spin coupling was not observed in the rare-earth metals, we consider that some quenching of the orbital angular moment occurs in the carbides owing to proximity of the acetylide ion and the development of covalent bonding.

In samarium and ytterbium dicarbides we have previously indicated the attainment of bivalent states by these lanthanons, and this now appears confirmed by the Bohr magneton numbers for SmC_2 ($>Sm^{3+}$) and YbC_2 ($<Yb^{3+}$). Sm^{2+}, being isoelectronic with Eu^{3+}, will have $\mu_{eff.} \simeq 3{\cdot}0$—$3{\cdot}5$; Yb^{2+}, isoelectronic with Lu^{3+}, should have $\mu_{eff.} \simeq 1{\cdot}0$. A proportion of bivalent ions in the carbides of these elements is to be compared with their metallic constitutions, which are also considered [6] to contain 2^+ ions.

Carbide	$\mu_{calc.}$	$\mu_{obs.}$	C	θ	Carbide	$\mu_{calc.}$	$\mu_{obs.}$	C	θ
Ce	2·56	2·19	0·59	−61°	Tb	9·70	9·57	11·36	−91·2°
Pr	3·62	3·15	1·35	+5·2	Dy	10·60	10·53	13·75	−68·9
Nd	3·68	3·53	1·55	+40	Ho	10·60	10·47	13·59	−25·6
Sm	1·65	2·85	1·01	−139	Er	9·6	8·75	9·49	+14·7
Gd	7·94	7·59	7·14	+41·3	Yb	4·6	3·69	1·69	−388

[3] Slater, *Phys. Rev.*, 1928, **32**, 349; 1930, **36**, 57.
[4] Van Vleck, "Theory of Electrical and Magnetic Susceptibilities," Oxford, 1932.
[5] Trombe, *Compt. rend.*, 1945, **221**, 19; **1953**, 236, 591; *J. Phys. Radium*, 1951, **12**, 22.
[6] Klemm and Bommer, *Z. anorg. Chem.*, 1937, **231**, 138.

Experimental. Carbides were prepared as in the preceding paper. After removal of excess of carbon, crushing to 100 mesh, and drying, the carbides were sealed in individual capillary tubes and magnetic susceptibilities were measured on a Gouy-type balance as previously described,[5] from the temperature of liquid nitrogen up to 500° K.

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105. *Rare-earth Carbides. Part III.* X-Ray Absorption.*

By R. C. VICKERY, R. SEDLACEK, and ARDYS RUBEN.

K-Edge absorption of some rare-earth carbides has been studied in further attempts to rationalise the structure of these compounds. The attainment of bivalent states in samarium and ytterbium carbides receives further confirmation, and from consideration of energy values the "free electron" concept appears substantiated.

POLARISING field effects upon 4*f* transitions in the lanthanons have been studied through the visual absorption spectrum,[1] and similar perturbation effects at the *K* and *L* levels have been observed in compounds of other elements by *X*-ray absorption techniques.[2] *X*-Ray absorptions of the rare-earth carbides were initially studied to elucidate anomalies

TABLE 1. *Comparison of wavelength and energy values for* K*-absorption edges of rare-earth metals and carbides.*

		Calc.*		Observed			
Element	Compound	$K\lambda$ (Å)	K_E (kev)	$K\lambda$ (Å)	K_E (kev)	ΔK (Å)	ΔE (kev)
Sc	Metal	2·751	4·496	2·795	4·435		
	Monocarbide			2·795	4·435	0·0	0·0
Y	Metal	0·726	17·037	0·725	17·103		
	Dicarbide			0·718	17·258	0·0065	0·155
La	Metal	0·318	38·931	0·318	38·982		
	Dicarbide			0·307	40·379	0·011	1·397
Ce	Metal	0·306	40·449	0·308	40·248		
	Dicarbide			0·301	41·184	0·007	0·936
Pr	Metal	0·295	41·998	0·292	42·453		
	Dicarbide			0·286	43·344	0·006	0·891
Nd	Metal	0·285	43·571	0·285	43·496		
	Dicarbide			0·280	44·273	0·005	0·777
Sm	Metal	0·264	46·846	0·263	47·135		
	Dicarbide			0·263	47·135	0·0	0·0
Gd	Metal	0·246	50·229	0·248	49·985		
	Dicarbide			0·244	50·805	0·004	0·820
Tb	Metal	0·238	51·998	0·237	52·305		
	Dicarbide			0·235	52·751	0·002	0·446
Dy	Metal	0·230	53·789	0·234	52·976		
	Dicarbide			0·231	53·664	0·003	0·688
Ho	Metal	0·222	55·615	0·219	56·605		
	Dicarbide			0·219	56·605	0·0	0·0
Er	Metal		57·483	0·214	57·927		
	Dicarbide			0·214	57·927	0·0	0·0
Yb	Metal	0·202	61·303	0·200	61·982		
	Dicarbide			0·197	62·926	0·003	0·944

* Fine and Hendel, *Nucleonics*, 1955, **13**, No. 3, 36; Bragg and Bragg, "The Solid State," Bell, London, 1949, p. 318.

in powder-diffraction studies (Part I), but have now been more directly applied in structure determinations.

Morehouse [3] showed the effect of variation in valency upon the absorption coefficient

* Parts I and II, preceding papers.

[1] Vickery, *J. Mol. Spectroscopy*, June, 1958; Halleck and Eckardt, *Z. Naturforsch.*, 1953, **8a**, 660; Boulanger, *Ann. Chim.*, 1952, **7**, 732.

[2] Cotton and Ballhausen, *J. Chem. Phys.*, 1956, **25**, 617; 1957, **26**, 1758; Kauer, *Z. phys. Chem. (Frankfurt)*, 1956, **6**, 105; Manescu, *Compt. rend.*, 1947, **225**, 537; Vainshtein, *Bull. Acad. Sci. U.R.S.S., Classe Sci. Chim.*, 1944, 382.

[3] Morehouse, *Phys. Rev.*, 1927, **29**, 767, 924.

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for an element, and Owen and Williams[4] also demonstrated the effects of chemical combination upon *X*-ray absorption spectra. Such studies are of increasing frequency, and the fine structures of *K* and *L* absorption edges have permitted some assumptions to be made on the effects of association upon energy transfers at these levels.[5]

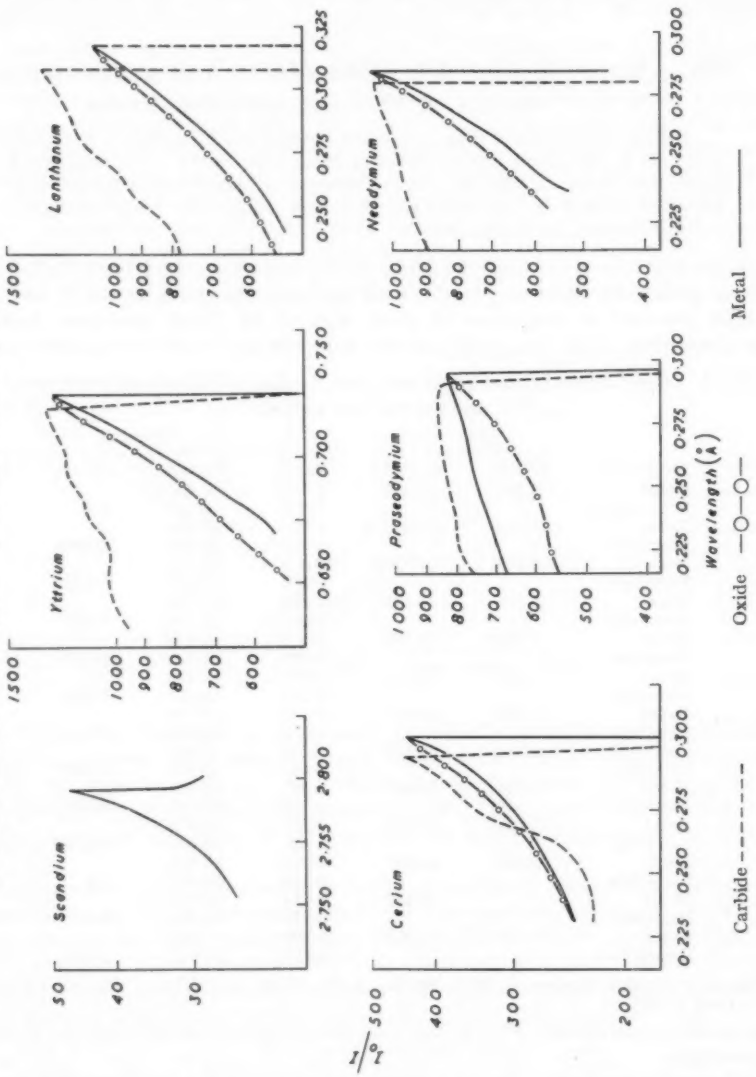

FIG. 1*a*. K-Absorption edges for rare-earth metals, oxides, and carbides.

We have now examined the *X*-absorption spectra at the *K* level (up to *ca.* 3 Å) of some rare-earth carbides and, as can be seen from Figs. 1*a* and 1*b*, structures of the *K*-absorption

[4] Owen and Williams, *Proc. Roy. Soc.*, 1931, *A*, **132**, 282.

[5] Rudstrom, *Arkiv Fys.*, 1957, **12**, 259, 287; Vainshtein, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 1196; Leder, *Phys. Rev.*, 1956, **101**, 1460; Cauchois, *J. Phys. Radium*, 1952, **13**, 113; Hill, Church, and Milhelich, *Rev. Sci. Instr.*, 1952, **23**, 523.

edges differ markedly from those of the corresponding metals and oxides. Absorption-edge wavelengths now determined for the metals and carbides together with energy values and differentials are given in Table 1.

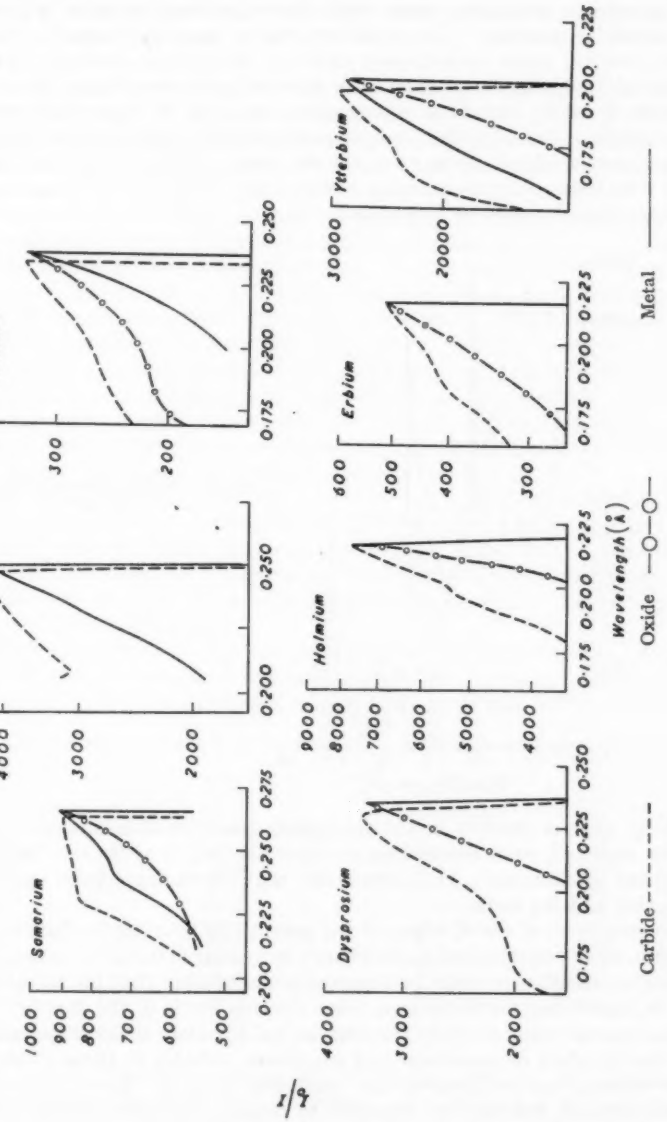

FIG. 1b. *K-Absorption edges for rare-earth metals, oxides, and carbides.*

Some *L*-absorption spectra have also been superficially examined, but at this level perturbation makes interpretation too complex to be attempted. Fig. 2 compares the gadolinium carbide *L*-absorption spectrum with that of the oxide. We have not studied reflection absorption in the visible region but, from the results now obtained, one would

expect the absorption spectra between, *e.g.*, 300 and 600 mμ to exhibit even grosser distortion and perturbation than hitherto observed.[1]

Qualitative aspects of the *K*-absorption spectra are: scandium carbide, oxide, and metal show the same pattern; that the carbide *K*-edge does not shift as in some of the other carbides is interesting since, with fewer shielding electrons, a greater perturbing effect might be expected. The small ionic size of scandium, however, leads to a higher electron density, which undoubtedly increases the overall shielding. Although the fine structure of the *K* edge for yttrium oxide differs slightly from that of the metal, the carbide absorption is widely variant at wavelengths below the *K* edge, which itself is shifted to shorter values. This edge-shift is again somewhat less than might be expected in view of the absence of shielding electrons in the 6th, 5th, and 4*f* orbitals; the shift is, however, greater than that seen in dysprosium carbides (Dy being of similar ionic radius to Y), but the energy differential is, of course, less.

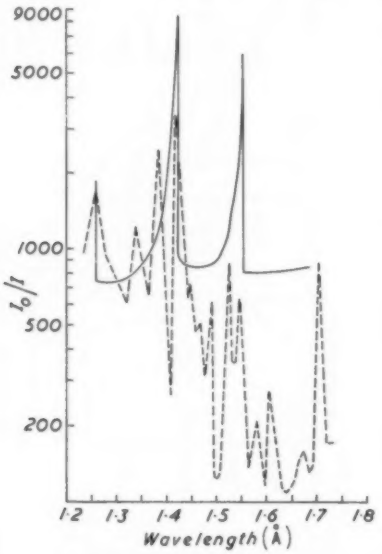

FIG. 2. *L-Absorption spectra of* Gd_2O_3 (——) *and* GdC_2 (– – –).

K-Edge shift is greatest in the absorption spectrum of lanthanum carbide, and this might be expected, since the lanthanum ion is the largest of the rare earths and possesses no shielding 4*f* electrons. The carbide fine edge shows appreciable variation from those of the oxide and the metal.

Fine structures of the *K* edges of the potentially bivalent lanthanons, samarium and ytterbium, show some similarity, absorbancy increasing in the order oxide < metal < carbide. Higher absorbancy might be expected in the bivalent than the tervalent state because of the increased electron density at lower electron levels in the former. Samarium and ytterbium metals being partially bivalent, we feel therefore the position and approximation of the fine *K* edges of samarium and ytterbium carbides to those of their metals to be further evidence that the bivalent state is adopted in them. Europium and its compounds were not studied, but may be expected to display absorption characteristics similar to those of the samarium compounds.

In conformity with the above, one would expect in higher-valency compounds the lessened electron shielding at lower orbits to effect lower absorbancies than in the lower-valency state of the same element. This relationship is generally shown in the *K* spectra of cerium, praseodymium, and terbium oxides and carbides, but the relationship of the

metal absorption curves to those of the compounds is anomalous. This anomaly is accentuated by the appearance of the cerium spectra at very low wavelengths, and the overall disposition of the cerium and terbium spectra which appears to suggest, very incongruently, that the metal has a higher valency than the oxide. In this context therefore it is clear that the relationship between the K absorption spectra of cerium, praseodymium, and terbium and those of their oxides and carbides is anomalous in comparison with those of the other rare earths.

That ionic size and electron density are factors in shielding the K shell from perturbation appears from the lack of K-edge shift from holmium onwards. The K-absorption edge for ytterbium carbide does shift, but this is attributed to the development of bivalency in this compound, giving a larger ionic radius for ytterbium and thus a lower electron density.

Absorption curves are essentially probability functions, showing variations in the probability of transitions at given energy levels, and much of the influence of bonding and atomic states is demonstrated in the edge structure, which is related to the number and nature of the nearest neighbours as well as the interatomic distances. It is not yet possible, however, to do more than deduce from these edge structures the above qualitative views.

In the Figures, the abscissæ are given in Ångström units for qualitative convenience. In Table 1 the wavelengths have been converted into energy units (kev) by using DuMond and Cohen's equation,[6] E (kev) $= 12{\cdot}3964/\lambda$ Å, and differentials are tabulated for the K-energy levels of the metals and carbides. Also given are K critical absorption-energy values listed by Fine and Hendel [7] for the rare-earth metals. As is seen, agreement of values now obtained and those calculated is reasonable (*ca.* 1%).

Since the energy differentials observed essentially represent the excess of energy required to transfer an inner-shell electron in the carbides to the first empty shell above that required for the same transition in the metals, it is suggested that, in the carbides, the 5*d* electron is the "free electron" required by Stackelberg's theory (see Parts I and II, preceding papers) so that the liberated K electron has to migrate to the 6*s* level before finding a suitable resting place.

Absorption coefficients at the K edge have been calculated through the usual equation, $I = I_0 e^{-\mu T}$, and are given in Table 2 for both metals and carbides. All absorption curves and absorption coefficients have been related to identical rare-earth contents.

TABLE 2. *Rare-earth metal and carbide absorption coefficients at* K*-absorption edge.*

Element	Compound	I_0/I	μ	Element	Compound	I_0/I	μ
Sc	Metal	49·5	26·01	Gd	Metal	440	40·59
	Monocarbide	49·5	26·01		Dicarbide	435	40·51
Y	Metal	1,350	48·06	Tb	Metal	352	39·10
	Dicarbide	1,348	48·05		Dicarbide	355	39·16
La	Metal	1,140	46·94	Dy	Metal ...	3,500	54·42
	Dicarbide	1,320	47·93		Dicarbide	3,500	54·42
Ce	Metal	460	40·88	Ho	Metal	8,000	59·93
	Dicarbide	470	41·03		Dicarbide	8,000	59·93
Pr	Metal	865	45·09	Er	Metal	525	41·77
	Dicarbide	860	45·06		Dicarbide	525	41·77
Nd	Metal	1,012	46·13	Yb	Metal	29,500	68·63
	Dicarbide	1,013	46·14		Dicarbide	30,000	68·74
Sm	Metal	920	45·51				
	Dicarbide	930	45·58				

In general, we consider that our data establish, with some certainty, that the structure assumed for the rare-earth dicarbides by Stackelberg [8] and Spedding *et al.*[9] is correct for all the carbides studied except for those of scandium, samarium, and ytterbium (and probably also europium). In the potentially bivalent elements it appears that the carbides

[6] DuMond and Cohen, *Phys. Rev.*, 1951, **82**, 555.
[7] Fine and Hendel, *Nucleonics*, 1955, **13**, No. 3, 36.
[8] Stackelberg, *Z. phys. Chem.*, 1930, *B*, **9**, 437.
[9] Spedding *et al.*, *J. Amer. Chem. Soc.*, 1958, **80**, 1804.

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closely approach ionic compounds, but if so then they should no longer be electrically conducting. The problem of their structure, therefore, still remains. Similarly, with scandium, Hume-Rothery gave evidence [10] that scandium carbide could be an interstitial compound, and the crystal structure (Part I) appears to confirm this, since the metal itself has a hexagonal habit, and it is unlikely that the intrusion of relatively small amounts of carbon will markedly alter this.

Experimental

The carbides were prepared as in Part I. Specimens were prepared for *X*-ray absorption studies by screening the carbides through a 100-mesh sieve under an inert solvent, replacing the solvent with ether, and evaporating the ether under vacuum. The fine carbide powders were then pressed into a filter holder so milled that the depth of penetration was approximately 1 mm. The actual depth was determined micrometrically, and the other dimensions of the aperture were accurately known. The specimen was sealed into the filter holder with acetate tape, and corrections were made for void space in the sample.

X-Irradiation was effected in the usual way, with a two-crystal spectrometer and Geiger recording at quarter-degree intervals, equivalent wavelengths being determined through the Bragg equation, $n\lambda = 2d \sin \theta$. A tungsten target tube with stabilised power supply supplied the radiation. Standard radiation (blank) and transmitted intensity were determined initially by direct counting, but later the Geiger counters were connected to a differential counter, incident radiation intensity being kept constant at 50,000 $\pm$ 100 c.p.min. I_0/I values were obtained directly, and absorption coefficients determined through the appropriate formulæ. Check comparisons were made on known, pure elements as standards, and absorption curves were plotted as the mean of several—usually six—determinations at given points.

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[*Received, July 17th*, 1958.]

[10] Hume-Rothery, *Phil. Mag.*, 1953, **44**, 1154.

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106. *Magnetic Susceptibilities of Praseodymium and Terbium Oxides.*

By R. C. Vickery and Ardys Ruben.

Magnetic susceptibility–temperature measurements below 300° of three oxides of praseodymium and three of terbium over a range of temperature yield magnetic moments for Pr_2O_3, Pr_6O_{11}, and PrO_2 of 3·55, 2·77, and 2·51 Bohr magnetons respectively and for Tb_2O_3, Tb_4O_7, and Tb_6O_{11} of 9·62, 8·70, and 8·49. The Curie–Weiss law is obeyed. The values agree well with theoretical ones for the proposed formula.

We have determined the magnetic susceptibility, over a range of temperature, of praseodymium and terbium oxides. *X*-Ray diffraction patterns have been prepared for each oxide studied, and lattice constants determined.

Magnetic Susceptibility.—The few data on the magnetic behaviour of these oxides deal predominantly with praseodymium oxides. Terbium oxides are less well characterised, probably owing in part to lack of pure materials.

The first studies on praseodymium oxides by Cabrera and Duperier [1] and Velayos [2] indicated that Pr_2O_3 and Pr_6O_{11} followed a modification of the Curie–Weiss law, $(\chi + k) = C/(T - \theta)$, where k represents a small positive susceptibility which is independent of temperature. Subsequently Rabideau [3] and LaBlanchetais [4] showed that Pr_2O_3 followed

[1] Cabrera and Duperier, *Compt. rend.*, 1929, **188**, 1640.
[2] Velayos, *Anales espan. Fis. Quim.*, 1935, **33**, 5.
[3] Rabideau, *J. Chem. Phys.*, 1951, **19**, 874.
[4] LaBlanchetais, *J. Rech. Centr. Nat. Rech. Sci.*, **6**, No. 29, 103—133.

the Curie–Weiss law, $\chi = C/(T - \theta)$, over a wide range of temperature and that Pr_6O_{11} did so only between 200° and 300° K. Rabideau's work is the only systematic study of the magnetic behaviour of all three praseodymium oxides and, in general, our work confirms his temperature-susceptibility data.

Whilst values for the magnetic moment of the Tb^{3+} ion in the sulphate and nitrate are given in the literature, the oxides Tb_2O_3 and Tb_4O_7 have been studied only by LaBlanchetais,[4] and, to our knowledge, no susceptibility data have been reported on Tb_6O_{11}. LaBlanchetais's work covers the temperature range from the b. p. of liquid nitrogen to room temperature; we have carried measurements up to 600° K.

The results obtained at 296° K are in Table 1. $10^6\chi_g$ values listed are for gram-susceptibilities of the oxides and $10^3\chi_M$ susceptibilities per g.-atom of rare-earth metal in c.g.s. units, the latter having been corrected for diamagnetic effects by use of values of -13×10^{-6} per gram-atom of oxygen and -38×10^{-6} for the diamagnetic contribution of the rare-earth ions.[3] This leads to corrections (in units of 10^{-6} per gram-atom of rare earth) of 58, 62, and 64 for the praseodymium oxides and 58, 61, and 62 for the terbium oxides.

TABLE 1. *Susceptibilities of oxides.*

	Specific susceptibility, obs.	Susceptibility per g.-atom	Comparative susceptibilities	
Formula	($10^6\chi_g$)	($10^3\chi_M$)	($10^6\chi_g$)	Ref.
Pr_2O_3	26·4	4·41	26·8	3
Pr_6O_{11}	14·6	2·54	14·3	3
PrO_2	10·7	1·91	10·75	3
Tb_2O_3	195·5	35·8	213·8	4 *
Tb_4O_7	160·7	30·1	188·7	4 *
Tb_6O_{11} ...	145·0	27·4	—	

* At 288·1° K.

The variation of susceptibility with temperature for the praseodymium system is given in Fig. 1. From 200° to 300° K the graphs can be represented by the equation, $1/\chi_M = C(T - \theta)$, where θ and C have the values in Table 2. From these constants the magnetic moments μ_B were calculated from the formula, $\mu_B = 2{\cdot}839\ [\chi_M(T - \theta)]^{\frac{1}{2}}$, and found to be in good agreement with those of other workers as well as close to the theoretical values predicted by Van Vleck and Frank.[5]

TABLE 2. *Magnetic moment data.*

	Observed values							
	Authors'			Other workers'				Theory
Formula	C	θ	μ_B	C	θ	μ_B	Ref.	μ_B
Pr_2O_3	1·55	−57	3·55	1·662	−64	3·61	4	3·62
				1·575	−55	3·55	3	
Pr_6O_{11}	0·957	−85	2·77	—	—	2·8	3	2·96
PrO_2	0·78	−127	2·51	0·769	−104	2·48	3	2·56
Tb_2O_3	11·49	−24	9·62	11·73	−12·7	9·72	4	9·70
Tb_4O_7	9·38	−19	8·70	10·38	−9·5	9·14	4	8·86
Tb_6O_{11} ...	8·94	−32	8·49	—	—	—		8·57

TABLE 3. *Formulæ of oxides.*

Classical formula	Active oxygen (%)	Ratio, oxygen : metal	Actual formula	Classical formula	Active oxygen (%)	Ratio, oxygen : metal	Actual formula
Pr_2O_3 ...	0·019	1·502	$Pr_2O_{3\cdot004}$	Tb_2O_3 ...	0·028	1·53	$Tb_2O_{3\cdot06}$
Pr_6O_{11} ...	3·16	1·836	$Pr_6O_{11\cdot02}$	Tb_4O_7 ...	2·19	1·756	$Tb_4O_{7\cdot03}$
PrO_2 ...	4·52	1·99	$PrO_{1\cdot99}$	Tb_6O_{11}...	2·75	1·82	$Tb_6O_{10\cdot92}$

Above 300° K the Curie–Weiss relationship no longer holds, and variations of $1/\chi_M$ with T, while linear, no longer give the same values of θ and C. Rabideau reports a definite curvature even below 300° K for Pr_6O_{11} but does not report data above this temperature.

[5] Van Vleck and Frank, *Phys. Rev.*, 1929, **34**, 1494, 1625.

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LaBlanchetais measured Pr_2O_3 up to 900° K and found a linear representation up to 680° K. The discontinuities in slope observed are real, and not attributable to instrumental error, as they are not shown in similar studies on similar materials with the same equipment.

Although it might be assumed that for Pr_2O_3 a structural transformation takes place in the neighbourhood of room temperature, yet there is no *X*-ray evidence to support this theory, and we have, therefore, no satisfactory explanation for these discontinuities.

Fig. 2 gives the temperature-susceptibility curves for the terbium oxides, and Table 2 the values for *C*, θ, and μ_B, calculated from the plot between 100° and 300° K. Again, discontinuities are observed around room temperature. Measurements have been made both with rising and with falling temperature, but the same plot was obtained either way.

FIG. 1. *Reciprocal susceptibility as a function of temperature.*

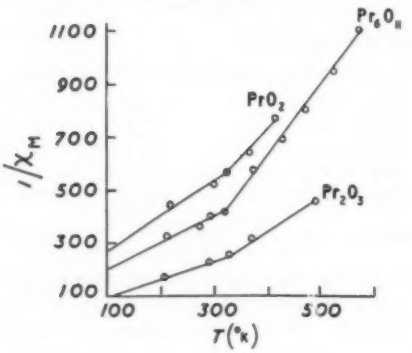
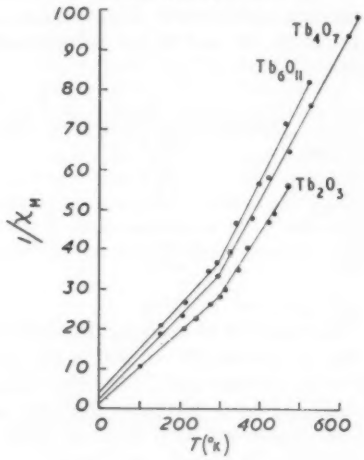


FIG. 2. *Reciprocal susceptibility as a function of temperature.*



The calculated magnetic moments are again in good agreement with theoretical values. Whilst our results are 1—2% lower than theory, LaBlanchetais's are up to 4% higher. In both cases, this is probably due to minor impurities in the starting materials. Our Tb_4O_7 was 99% pure and, although not indicated by spectroscopic analysis, might contain small amounts of gadolinium and/or yttrium which would lower the susceptibilities.

LaBlanchetais's material contained 92—94% of terbium oxide, and her results should therefore deviate more widely from theory. Also, as mentioned by Cabrera and Duperier,[1] absorption of water by terbium salts can appreciably reduce the *C* value.

The observed moments for Pr^{3+} and Pr^{4+} agree well with those of other workers as well as with theoretical values. The magnetic behaviour is consistent with the Curie–Weiss law for all three praseodymium oxides below 300° K, but not above it.

A moment of 2·77 Bohr magnetons for Pr_6O_{11} agrees well with a theoretical value of 2·96 calculated for $Pr_2O_3,4PrO_2$, and with Rabideau's calculated moment of 2·86 Bohr magnetons.

The observed magnetic susceptibilities for terbium are close enough to give some information about possible formulæ for Tb_4O_7 and Tb_6O_{11}. Assuming, according to the Sommerfeld–Kossel rule, the moment for Tb^{4+} to be equal to that for Gd^{3+}, we expect the magnetic moment of Tb_4O_7 (based on the formula, $Tb_2O_3,2TbO_2$) to be 8·86 Bohr magnetons, and for Tb_6O_{11} (equivalent to $Tb_2O_3,4TbO_2$), 8·57 μ. Our observed moments are 98·2 and 99·1% of these respectively. Such close agreement does we feel, substantiate the formulæ proposed.

X-Ray Diffraction.—Two forms of Pr_2O_3 have been reported,[6] a yellow low-temperature "*C*" cubic structure and a green high-temperature "*A*" hexagonal structure. Our material was light green, and lines from both the cubic and the hexagonal structure were observed in the *X*-ray pattern. The cubic form predominated, however, and gave a value of 5·61 Å for the lattice constant.

The *X*-ray powder pattern of Pr_6O_{11} showed only the lines of a cubic face-centred compound with a cell edge of 5·45 Å.

The pattern for PrO_2 was very similar to that for Pr_6O_{11}, differing only in yielding a smaller cell size, 5·38 Å. Although no standard is listed for PrO_2 in the A.S.T.M. index, our result compared favourably with the value obtained by McCullough [7] of 5·39 Å and with that of 5·38 Å obtained by Gruen, Koehler, and Katz.[8]

All the *X*-ray diffraction patterns for the terbium oxides can be indexed on the basis of face-centred cubic cells. Tb_2O_3 has a cell edge of 5·33 Å, and Tb_4O_7, 5·28 Å. Although Guth and Eyring [9] believe there to be no evidence for Tb_4O_7 and report instead $TbO_{1·74}$ with a rhombohedral lattice, Gruen *et al.*[8] list Tb_4O_7 as face-centred cubic, with $a_0 = 5·29$ Å.

The *X*-ray diffraction pattern for Tb_6O_{11} consists of a single phase which is face-centred cubic with a cell constant of 5·26 Å. Gruen *et al.*[8] report the formation of Tb_6O_{11} with a Tb : O ratio of 1 : 1·83 and a cell constant of 5·265 Å. However, Guth and Eyring [9] consider that the highest state of oxidation obtained is $TbO_{1·81}$, with a cell constant of 5·286 Å.

Experimental.—Preparation of oxides. Pr_6O_{11} was purchased from the Lindsay Chemical Company as 99·8% pure, and Tb_4O_7 from the Michigan Chemical Company as 99% pure. All oxide used was first dissolved in acid, precipitated as oxalate, and ignited at 650° c.

The sesquioxides of both praseodymium and terbium were prepared by heating the air-ignited oxide in a stream of dry hydrogen for 2 hr. at 900° c. Even at 900° only a small amount of oxide could be reduced at one time, although both Guth and Eyring [9] and Gruen, Koehler, and Katz [8] report that reduction occurred readily between 600° and 650° c.

McCullough's [7] sodium chlorate–pressure technique was used to prepare the higher oxides, PrO_2 and Tb_6O_{11}. The production of PrO_2 proceeded readily with an oxygen pressure of about 50 atm. However, even at 60—75 atm. it was not possible to oxidise tervalent terbium completely to the 4+ state, the highest oxide obtained appearing, by "active oxygen" analysis, to be Tb_6O_{11}.

"Active oxygen" analysis. All the oxides prepared were analysed for active oxygen by the method of Barthauer and Pearce; [10] from the active oxygen content the oxygen-to-metal ratio was calculated, and the corresponding formula determined. These results are listed in Table 3.

X-Ray diffraction patterns were obtained with a General Electric XRD powder camera with a radius of 14·32 cm. using Co-K_α radiation at 50 kv and 6 ma with an iron filter. Exposure of 4 hr. was standard.

The apparatus and procedure employed for measurement of magnetic susceptibility has been reported previously [11] and will not be repeated in detail. A Gouy-type assembly was employed using a magnet field strength of 3340 gauss with appropriate standardisation and correction for container paramagnetism. Temperatures higher than 25° c were obtained by a small heating unit between the magnet poles which, for low temperatures, was replaced by a double-jacketed vacuum flask containing solid carbon dioxide, ice, liquid nitrogen, etc. The powder susceptibility data obtained are considered to have an accuracy of ±1·5%.

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[6] McCullough and Britton, *J. Amer. Chem. Soc.*, 1952, **74**, 5225.
[7] McCullough, *ibid.*, 1950, **72**, 1386.
[8] Gruen, Koehler, and Katz, *ibid.*, 1951, **73**, 1475.
[9] Guth and Eyring, *ibid.*, 1954, **76**, 5242.
[10] Barthauer and Pearce, *Ind. Eng. Chem., Anal. Ed.*, 1946, **18**, 479.
[11] Vickery and Klann, *J. Chem. Phys.*, 1957, **27**, 1161.

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107. *The Structure of* cyclo*Eucalenol.*

By J. S. G. Cox, F. E. King, and T. J. King.

Further investigation of the triterpene *cyclo*eucalenol, already recognised as a near analogue of *cyclo*artanol, has now defined it as 4β-demethyl-24-methylene*cyclo*artanol. The crucial experiment was the methylation of 24-demethyl*cyclo*eucalanone which gave *cyclo*artanone by introducing a single methyl group at $C_{(4)}$.

*cyclo*EUCALENOL was discovered in tallow-wood (*Eucalyptus microcorys*) and shortly afterwards in *Erythrophloeum guineense*,[1] and our early investigations disclosed its general resemblance to the tetracyclic triterpenes. In particular it appeared to contain (i) a *cyclo*propane ring, which from the nature of oxidation products probably involved $C_{(9)}$; (ii) a methylene substituted grouping, $\cdot CH_2 \cdot C(:CH_2) \cdot CHMe_2$, believed to be part of a side-chain $\cdot CHMe \cdot CH_2 \cdot CH_2 \cdot C(:CH_2) \cdot CHMe_2$; and (iii) a 3β-hydroxyl group. However, removal of the side-chain methylene group did not give *cyclo*artanol (I), and the enedione formed by oxidation of the acid-isomerised 24-demethyl*cyclo*eucalanyl acetate was not identical with 7 : 11-dioxolanost-8-enyl acetate (II; R = Me, R′ = COMe).

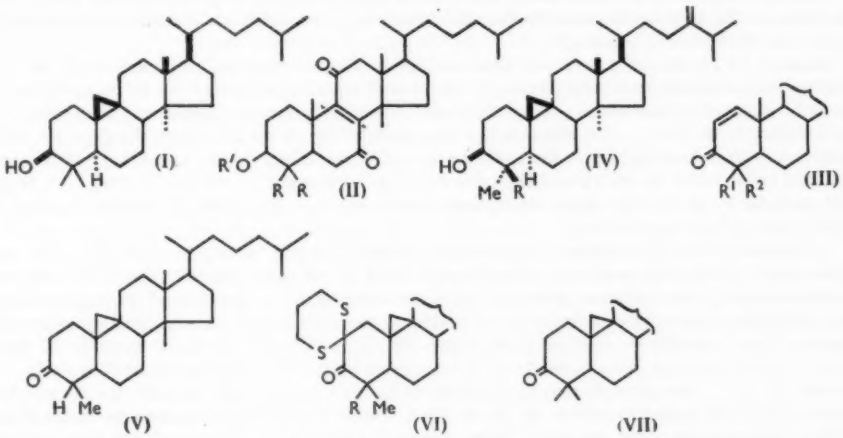
It was the underlying assumption of further work that *cyclo*eucalenol had the conventional perhydro*cyclo*pentanophenanthrene nucleus. On this hypothesis it is readily established that position 14 is substituted, otherwise, by analogy with sterols, opening of the *cyclo*propane ring and oxidation of the product (eucalenyl acetate) would afford a *cisoid* 8(14)-ene-7 : 15-dione readily distinguishable from the *transoid* enedione actually obtained.[1,2] A further indication of the lanostane rather than euphane configuration at $C_{(13)}$ and $C_{(14)}$ is the formation from the previously described epoxyeucalenyl acetate of a product with the characteristic ultraviolet absorption of a 7 : 9(11)-diene of the lanostane series.[3]

The first significant difference between *cyclo*eucalanol and the normal tetracyclic triterpenes was observed in its reaction with phosphorus pentachloride. Instead of the usual A-ring contraction leading to an *iso*propylidene compound, a stable chloride was obtained in high yield, comparable in the unreactivity of its halogen atom with cholesteryl chloride. A similar chloro-compound was likewise derived from eucalenol thus eliminating the possibility that the *cyclo*propane unit was the origin of the unusual reaction with phosphorus pentachloride. It seemed probable therefore that the anomaly derived from incomplete substitution of the $C_{(4)}$ position and a quantitative bromination of eucalanone, in which four molecules of bromine were consumed, appeared to confirm this explanation. The only isolable product, however, was an unstable tribromo-αβ-unsaturated ketone, and although superficially in agreement with presence of the unit $\cdot CH_2 \cdot CO \cdot CH_2 \cdot$, earlier work on cholestanone–bromine reactions does not support the view that a grouping of this type would necessarily react with four molecules of halogen.[4] The nature of the bromination product remains unproved but its formation obviously gives evidence of the abnormal structure of the A-ring. Very recently [5] Djerassi and Burstein have shown that a derivative of iresin having a 4-monomethylated 3-oxo ring A, and also 4-methyldihydrotestosterone, give 2 : 6-dibromo-3-oxo-Δ^4-derivatives. It is thus possibe that the brominated eucalanone is a 2 : 2 : 6-tribromo-3-oxo-Δ^4-compound. A monobromoeucalanone was also obtained, and was transformed with boiling collidine into a product having ultraviolet absorption compatible with the 1-en-3-one structure (III). This unsaturated carbonyl group can occur only in ring A of the normal *cyclo*pentanophenanthrene terpenoids, but its formation

[1] Cox, King, and King, *J.*, 1956, 1384.
[2] Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold, New York, 3rd Edn., 1949, pp. 243, 248.
[3] Dorée, McGhie, and Kurzer, *J.*, 1949, 570; Barbour, Bennett, and Warren, *J.*, 1951, 2540.
[4] Crowne, Evans, Green, and Long, *J.*, 1956, 4351.
[5] Djerassi and Burstein, *J. Amer. Chem. Soc.*, 1958, **80**, 2593.

gives no indication of the $C_{(4)}$ substituents R^1 and R^2. The evidence of light-absorption measurements appears to support the possibility of incomplete alkylation at position 4 since the infrared spectrum of a *cyclo*eucalenyl acetate derivative with a degraded side-chain lacks the 1390 and 1365 cm.$^{-1}$ bands characteristic of the *gem*-dimethyl group. *cyclo*Eucalenol therefore appears to be either a 4-demethyl- or 4 : 4-bisdemethyl-24-methylene*cyclo*artanol (IV), but molecular-weight estimations by the usual methods were inadequate to differentiate between the alternative C_{29} and C_{30} formulæ. Nevertheless, *cyclo*eucalenol cannot be the 4 : 4-bisdemethyl-24-methylene*cyclo*artanol since the enedione from 24-demethyl*cyclo*eucalanyl benzoate would then be (II; R = H, R′ = COPh), *viz.* 3β-benzoyloxy-14-methylcholest-8-ene-7 : 11-dione, and a compound of this structure is known [6] and is clearly not identical with the analogous product from *cyclo*eucalenol. The crystallographic molecular-weight estimation was also unsuccessful in this case owing to imperfections in the crystals of *cyclo*eucalenol and of its derivatives, but volumetrically determined equivalents of *cyclo*eucalenyl hydrogen phthalate gave very consistent results favouring a C_{30} molecule, thus strongly supporting the structure (IV; R = H) monomethylated at position 4.

The constitution of *cyclo*eucalenol and its relation to *cyclo*artanol were finally established by methylation of the 24-demethyl*cyclo*eucalanone (V) by the method of Woodward, Patchett, Barton, Ives, and Kelly,[6] used by Beton, Halsall, Jones, and Phillips [7] for the



methylation of cholestanone. Formylation of the ketone readily gave a colourless hydroxymethylene derivative having the expected ultraviolet absorption, and by replacement of the formyl group the dithian (VI; R = H) was obtained, after chromatography, as a glassy resin. Methylation of the thio-compound afforded a product consisting of unchanged dithian (72%) and a more easily eluted crystalline material (23%). The recovered dithian was identified by reconversion into the crystalline demethyl*cyclo*eucalanone (V). The crystalline product, which exhibited the infrared carbonyl stretching frequency regarded as characteristic of a fully substituted ketone,[7] was readily converted into the corresponding ketone identical (m. p., mixed m. p., and infrared absorption) with *cyclo*artanone (VII). We are indebted to Professor F. S. Spring, F.R.S., for arranging these comparisons.

It is thus conclusively proved that 24-demethyl*cyclo*eucalanone is identical with 4-demethyl*cyclo*artanone and that one methyl group only is attached to position 4 in

[6] Barton, Ives, Kelly, Woodward, and Patchett, *Chem. and Ind.*, 1954, 605; Woodward, Patchett, Barton, Ives, and Kelly, *J.*, 1957, 1131.
[7] Beton, Halsall, Jones, and Phillips, *J.*, 1957, 753.

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*cyclo*eucalenol. It is possible to establish the orientation of this methyl group from the stability of the dithian (VI; R = H) to alkali, thus indicating its equatorial conformation. *cyclo*Eucalenol can therefore be unambigously described as 4β-demethyl-24-methylene-*cyclo*artanol (IV; R = H), as recorded in a recent preliminary communication.[8]

Professor Djerassi has measured the optical rotatory dispersion of *cyclo*eucalanone and finds it compatible with the structure now deduced, although in fact rotatory dispersion does not distinguish between cholestanone and either of its 4-monomethyl derivatives.

During the examination of specimens of the hydrocarbon (*cyclo*eucalane) obtained from *cyclo*eucalanyl chloride and from the corresponding ketone, certain discrepancies were observed which were finally attributed to the formation of mixed isomers during the reduction of the $C_{(24)}$ methylene group. Similar results have been noted in the reduction of polyporenic acid A.[9] Although this observation implies that the reported properties of *cyclo*eucalanol derivatives may refer to mixtures, the structural arguments are unaffected. Furthermore, no discrepancies were detected in the case of the *cyclo*eucalenyl chloride and *cyclo*eucalenone reduction products, which consisted of the identical homogeneous hydrocarbon, thus confirming that the formation of the chloride occurred without rearrangement of the nucleus.

Experimental

Optical rotations are recorded for chloroform solutions and sodium light at room temperature. Light petroleum refers to the fraction of b. p. 60—80°, and alumina for chromatography was P. Spence's Grade H.

Eucala-7 : 9(11)-*dienyl Acetate*.—Epoxyeucalanyl acetate [1] (610 mg.) in acetic acid (30 c.c.) with concentrated sulphuric acid (6 drops) was heated on a steam-bath for 1 hr., and then kept overnight at room temperature. Then the dark brown solution was diluted and the precipitate was collected with ether. The *diene acetate* was purified by chromatography on alumina, from which it was eluted by light petroleum–benzene (9 : 1), and then crystallised from chloroform–methanol as rhombs, m. p. 129—130°, [α] +93° (*c* 1·1) (Found: C, 81·8; H, 11·1. $C_{32}H_{52}O_2$ requires C, 82·0; H 11·2%), light absorption in ethanol: $\lambda_{max.}$ 236, 243, and 252 mμ (ε 14,800, 17,300, and 11,700, respectively).

Chlorination of cyclo*Eucalanol*.—(*a*) *cyclo*Eucalanol (1 g.) in light petroleum (350 c.c.) was shaken with excess of phosphorus pentachloride for 1 hr. at room temperature. The solution was then washed with aqueous sodium hydroxide and water and percolated through alumina from which benzene–light petroleum (1 : 4) eluted a chloro*cyclo*eucalone, crystallising as needles or prisms (from chloroform–methanol), m. p. 97—98°, [α] +37° (*c* 0·5) (Found: C, 80·6; H, 11·6; Cl, 8·1. Calc. for $C_{30}H_{51}Cl$: C, 80·6; H, 11·5; Cl, 7·9%). (*b*) *cyclo*Eucalanol (0·5 g.) in dry pyridine (5 c.c.) with phosphorus oxychloride (1·25 c.c.) was heated at 100° for 2 hr. The product was a chlorohydrocarbon, m. p. 97—98°, identical with that obtained by method (*a*).

The chloro-compounds obtained from different samples of *cyclo*eucalanol had slightly different properties, the m. p. varying from 92° to 104°. The chloro-compounds were unaffected by boiling collidine during 4 hr., or by boiling 20% methanolic potassium hydroxide during 3 hr.

A similar chloro-compound was obtained when the mixed isomers resulting from the action of acid on *cyclo*eucalanol were treated as in (*b*).

Eucalan-3-*one*.—Eucalanol [1] (also prepared by vigorous Huang-Minlon reduction of 7 : 11-dioxoeucalanyl acetate [1]) (500 mg.) was oxidised by chromic oxide (100 mg.) in acetic acid (20 c.c.) during 14 hr. at room temperature. The *ketone* (360 mg.) obtained from the reaction in the usual way separated from chloroform–methanol as plates, m. p. 132—134°, [α] +40° (*c* 2·7) (Found: C, 84·0; H, 12·3. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%). The *dinitrophenylhydrazone* separated from chloroform–methanol as orange plates, m. p. 252—254° (Found: C, 70·7; H, 8·9; N, 9·6. $C_{36}H_{56}O_4N_4$ requires C, 71·0; H, 9·3; N, 9·2%).

Bromination of Eucalanone.—Eucalanone (119·6 mg.) in acetic acid (10 c.c.) was mixed with a solution of bromine (200 mg.) in acetic acid (10 c.c.) with the addition of 2 drops of 50% hydrobromic acid–acetic acid, and kept at 35°. A blank solution identical with the above but for the absence of the ketone was simultaneously prepared. The uptake of bromine was

[8] Cox, King, and King, *Proc.*, 1957, 290.
[9] Jones and Woods, *J.*, 1953, 464.

measured volumetrically on aliquot portions of 1 c.c. by using thiosulphate. 4 mols. of bromine were absorbed after 72 hr.

The *product* obtained by diluting a similar bromination mixture after 72 hr. crystallised as colourless needles, turning yellow on exposure to light, m. p. 181—182° (decomp.), [α] −74° (*c* 1·8) (Found: C, 53·2; H, 6·9; Br, 37·0. $C_{30}H_{47}OBr_2$ requires C, 54·3; H, 7·1; Br, 36·1%), light absorption: $\lambda_{max.}$ 271 mμ (ε 12,000 in hexane).

2-Bromoeucalan-3-one.—Eucalanone (434 mg.) in acetic acid (30 c.c.) was mixed with a solution of bromine in acetic acid (1M; 1·1 c.c.) at room temperature. Next day the solution was diluted and the product was crystallised from chloroform–methanol giving *2-bromoeucalan-3-one* (337 mg.) as plates, m. p. 191°, [α] +47° (*c* 1·9) (Found: Br, 16·3. $C_{30}H_{51}OBr$ requires Br, 15·8%).

Eucal-1-en-3-one.—2-Bromoeucalanone (750 mg.) in collidine (5 c.c.) was heated under reflux for 4 hr. The solution was then diluted and the product collected in light petroleum. Chromatography over alumina afforded, in the benzene–light petroleum (1 : 1) fraction, *eucal-1-en-3-one* which crystallised from methanol in plates, m. p. 147—148° (Found: C, 84·5; H, 11·7. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%), light absorption: $\lambda_{max.}$ 229 mμ (ε, 9,400). The *dinitrophenylhydrazone* separated from chloroform–methanol as bright red plates, m. p. 255—257° (Found: C, 70·9; H, 8·8; N, 9·7. $C_{36}H_{54}O_4N_4$ requires C, 71·2; H, 9·0; N, 9·2%), light absorption: $\lambda_{max.}$ 260, 385 mμ (ε, 15,800, 28,300).

*24-Demethyl*cyclo*eucalanyl Benzoate.*—A mixture of demethyloxo*cyclo*eucalanyl acetate (4·9 g.) and anhydrous hydrazine (20 c.c.) in dry ethylene glycol (150 c.c.), containing sodium (3·2 g.), was heated under reflux for 14 hr. Worked up in the usual way, demethyl*cyclo*eucalanol was obtained in 87% yield. The *benzoate* crystallised from ethyl acetate–methanol as plates, m. p. 121—122°, [α] +91° (*c* 2·4) (Found: C, 83·2; H, 10·3. $C_{36}H_{54}O_2$ requires C, 83·3; H, 10·5%).

24-Demethyleucal-9(11)-enyl Benzoate.—A solution of the above benzoate (4·5 g.) in chloroform (350 c.c.) was treated with a stream of dry hydrogen chloride for 4 hr. The product crystallised from methanol as plates, m. p. 144—150°. This mixture (3·5 g.) in acetic acid (250 c.c.) was oxidised with chromic oxide (1·5 g. in 100 c.c. acetic acid) for 20 min. at 90°. The crude product, isolated in the usual way, was absorbed from light petroleum by alumina (200 g.). Elution of the column by light petroleum–benzene (9 : 1; 1 l. and 4 : 1; 2½ l.) afforded a fraction which crystallised from chloroform–methanol, giving *24-demethyleucal-9(11)-enyl benzoate* (650 mg.) as needles, m. p. 186—187°, [α] +104° (*c* 0·9) (Found: C, 83·3; H, 10·5. $C_{36}H_{54}O_2$ requires C, 83·3; H, 10·5%). The acetate [1] had [α] +83° (*c* 0·6).

24-Demethyl-7 : 11-dioxoeucal-8-enyl Benzoate.—Further elution of the above chromatogram with light petroleum–benzene (7 : 3) afforded, after crystallisation from chloroform–methanol, *24-demethyl-7 : 11-dioxoeucal-8-enyl benzoate* (370 mg.) as blades, m. p. 141—143°, [α] +125° (*c* 0·59) (Found: C, 79·2; H, 9·2. $C_{36}H_{50}O_4$ requires C, 79·1; H, 9·2%).

24-Demethyl-12-oxoeucal-9(11)-enyl Benzoate.—From the same column benzene eluted *24-demethyl-12-oxoeucal-9(11)-enyl benzoate* (450 mg.), which crystallised from methanol as needles, m. p. 223—224°, [α] +128° (*c* 2·8) (Found: C, 80·9; H, 9·7. $C_{36}H_{52}O_3$ requires C, 81·1; H, 9·8%).

24-Demethyleucalanol.—24-Demethyleucal-9(11)-enyl benzoate (430 mg.) in acetic acid (70 c.c.) was shaken at 80° for 24 hr. with platinum (from 800 mg. of platinic oxide) in an atmosphere of hydrogen. The product crystallised from methanol and was then hydrolysed to give *24-demethyleucalanol* (360 mg.) as plates (from chloroform–methanol), m. p. 154—155°, [α] +38° (*c* 0·6) (Found: C, 83·4; H, 12·2. $C_{29}H_{52}O$ requires C, 83·6; H, 12·6%).

cyclo*Eucalenyl Hydrogen Phthalate.*—*cyclo*Eucalenol and an equivalent amount of phthalic anhydride were heated at 100° in pyridine for 1 hr. The *product* crystallised from methanol in long, stout needles, m. p. 174°, [α] +80° (*c* 0·64) (Found: C, 79·1; H, 9·3. $C_{38}H_{54}O_4$ requires C, 79·4; H, 9·5%). The equivalent weight was determined by direct titration in aqueous alcoholic solution of the acid against approx. 0·1N-sodium hydroxide. About 500 mg. of acid were used in each titration and the values of five determinations were 572, 573, 576, 575, and 580, giving an average value of 575. The calculated equivalent is 574·8.

*24-Demethyl*cyclo*eucalan-3-one.*—24-Demethyl*cyclo*eucalanol [1] (2 g.) was oxidised overnight by a solution of chromic oxide (0·5 g.) in pyridine (20 c.c.). The mixture was worked up in the usual way and the *ketone* (1·8 g.) was obtained from methanol in plates, m. p. 109°, [α] +55° (*c* 2·3) (Found: C, 84·6; H, 11·9. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%). The *oxime* crystallised from aqueous ethanol as felted needles, m. p. 187° (Found: N, 3·2. $C_{29}H_{49}ON$ requires N, 3·3%).

2-*Hydroxymethylene*-24-*demethyl*cyclo*eucalan*-3-*one*.—24-Demethyl*cyclo*eucalan-3-one (2 g.) in ether (50 c.c.) was treated with sodium methoxide (from 1·5 g. of sodium) in methanol (15 c.c.) and ethyl formate (24 c.c.) for 4 days with occasional shaking. The mixture was neutralised with a buffered phosphate solution (pH = 8) and the product was collected in ether. The *hydroxymethylene derivative* (1·7 g.) crystallised in colourless prisms (from chloroform–methanol), m. p. 102°, [α] +94° (*c* 1·07) (Found: C, 81·5; H, 10·7. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%), light absorption: $\lambda_{max.}$, 289 mμ (ε, 7,500).

24-*Demethyl*-3-*oxo*cyclo*eucalane*-2-spiro-2′-(1′ : 3′-*dithian*).—2-Hydroxymethylene-24-demethyl*cyclo*eucalanone (1·3 g.) and trimethylene ditoluene-*p*-thiosulphonate (1·5 g.) in ethanol (40 c.c.) were treated with potassium acetate (4 g.) in ethanol (60 c.c.). The mixture was heated under reflux for 6 hr. and the solvent was then evaporated. The residue was extracted with light petroleum, and the resulting solution was filtered and passed down an alumina column (50 g.). The *dithian* (1·1 g.) was eluted from the column by benzene–light petroleum (1 : 4) and when the solvent was removed formed an amorphous, clear gum, [α] +160° (*c* 1·6) (Found: C, 74·2; H, 9·9. $C_{32}H_{52}OS_2$ requires C, 74·4; H, 10·1%), infrared absorption band at 1702 cm.$^{-1}$.

4-*Methyl*-24-*demethyl*-3-*oxo*cyclo*eucalane*-2-spiro-2′-(1′ : 3′-*dithian*).—The above dithian (1 g.) was heated under reflux in a mixture of benzene (15 c.c.) and a solution of potassium *tert.*-butoxide (from 0·3 g. of potassium) in *tert.*-butyl alcohol (15 c.c.). Excess of methyl iodide (2 c.c.) was added to the hot solution which was heated for a further 1 hr. Water was then added and the benzene layer was separated, and the aqueous layer extracted with ether. The combined extracts were evaporated and the residue was taken up in light petroleum. This solution was then passed down an alumina (50 g.) column from which, by elution with light petroleum–benzene (9 : 1), was obtained the *methylation product* (230 mg.) which crystallised from chloroform–methanol as needles, m. p. 168—170°, [α] +107° (*c* 1·2) (Found: C, 74·6; H, 10·3. $C_{33}H_{54}OS_2$ requires C, 74·7; H, 10·3%), infrared absorption band at 1689 cm.$^{-1}$.

Further elution of the column with light petroleum–benzene (4 : 1) afforded an amorphous fraction (720 mg.) which was identified as starting material by reconversion into demethyl*cyclo*eucalanone by the method used below. The identity was established by m. p., mixed m. p., and the identity of infrared absorption.

cyclo*Artanone*.—The above methylated dithian (120 mg.) in ethanol (10 c.c.) was heated under reflux with Raney nickel (1 g.) for 6 hr. The metal was removed, the solvent evaporated, and the residue treated overnight with a solution of chromic oxide (100 mg.) in pyridine (5 c.c.). The product (69 mg.), obtained in the usual way, crystallised from methanol in long, thin blades, m. p. 109°, [α] +25° (*c* 0·4) (Found: C, 84·2; H, 11·7. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%), the m. p. was not depressed by admixture with authentic *cyclo*artanone, and the infrared absorption of the product and of *cyclo*artanone were indistinguishable.

cyclo*Eucalenyl Chloride*.—*cyclo*Eucalenol (1 g.) in pyridine with phosphorus oxychloride (excess) at the boiling point for 2 hr. gave the *chloride* (0·8 g.) which was readily purified from chloroform–methanol as flattened needles, m. p. 106°, [α] +24° (*c* 0·95) (Found: C, 81·2; H, 11·1. $C_{30}H_{49}Cl$ requires C, 80·9; H, 11·1%).

cyclo*Eucalene*.—(*a*) The above chloride (0·5 g.) in *n*-butanol (50 c.c.) was treated, at the boiling point, with sodium (1 g.) until the metal had dissolved. Water was then added and the alcohol was removed by distillation in steam. The cyclo*eucalene* (0·4 g.) which remained crystallised from chloroform–methanol as needles, m. p. 71—72°, [α] +35° (*c* 0·76) (Found: C, 87·7; H, 12·1. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%). (*b*) A mixture of *cyclo*eucalenone (0·5 g.) and anhydrous hydrazine (2 c.c.) in ethylene glycol (15 c.c.) containing sodium (0·3 g.) was heated under reflux for 12 hr. The cooled solution was diluted and the product collected into ether. The ether was evaporated and the residual hydrocarbon crystallised from chloroform–methanol forming needles, m. p. 70—71° undepressed by the material prepared in (*a*).

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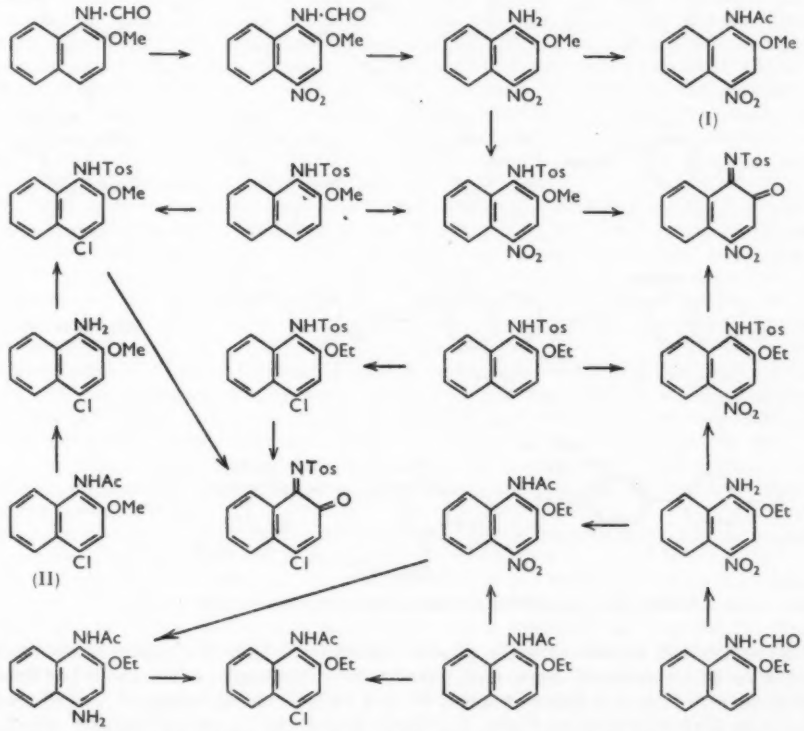
108. *Substitution Reactions with 2-Methoxy- and 2-Ethoxy-1-naphthylamines.*

By F. Bell.

Substitution experiments with the acetyl, formyl, and toluene-*p*-sulphonyl derivatives of 2-methoxy- and 2-ethoxy-1-naphthylamines show that, whereas chlorination and nitration proceed mainly, or even exclusively, in position 4, yet bromination may yield the 6-derivative as the main product.

A comparison is made with the results of substitution experiments with 2 : 6-xylidine.

Bradley and Robinson [1] showed that *N*-acetyl-2-methoxy-1-naphthylamine is nitrated at position 4, and Bell [2] showed that the same position is entered on chlorination. Davis [3] stated that both *N*-acetyl-2-methoxy- and -2-ethoxy-1-naphthylamine undergo bromination in position 6 exclusively. Other substitution products have been oriented only by analogy.



Scheme A. *Orientation of nitro-compounds based on* (I) *and of chloro-compounds based on* (II).
(Tos = $SO_2 \cdot C_7H_7$)

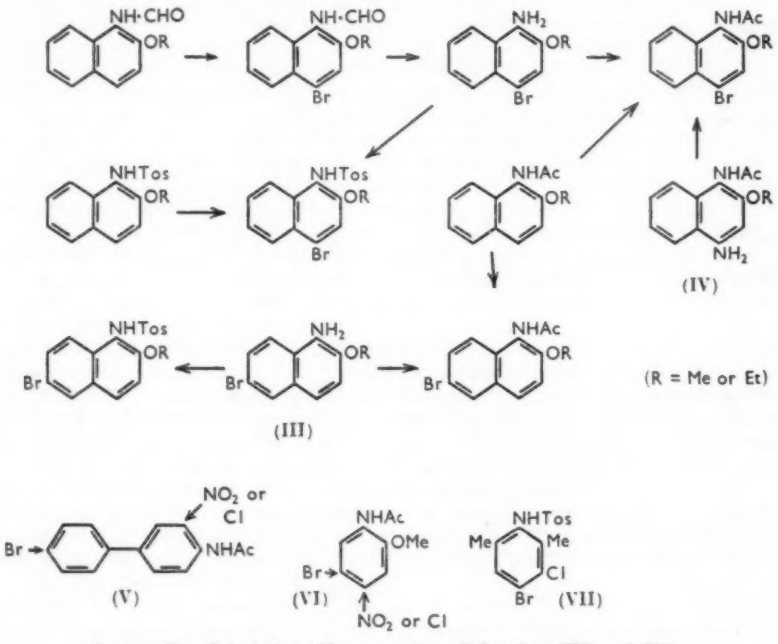
It was the present object to establish with certainty the structures of the already known substitution products and also to examine whether there really exists the marked

[1] Bradley and Robinson, *J.*, 1934, 1488.
[2] Bell, *J.*, 1954, 472.
[3] Davis, *Chem. News*, 1896, **74**, 302.

difference between nitration and chlorination on the one hand and bromination on the other which appears to emerge from the above experimental results.

The reactions set out in flow sheet (A) establish that nitration and chlorination of all derivatives examined occurs mainly or even exclusively in position 4. On the other hand, see flow sheet (B), the bromination of *N*-acetyl-2-methoxy-1-naphthylamine is complex; the main product was the 6-derivative accompanied by a small amount of the 4-derivative and another monobromo-compound not identical with the 3-derivative, which was synthesised from 3-bromo-1-nitro-2-naphthylamine.[4] Similarly, the bromination of *N*-acetyl-2-ethoxy-1-naphthylamine yielded the 6- and the 4-derivative, the latter in small amount. However, the bromination of 2-methoxy- and 2-ethoxy-*N*-formyl-1-naphthylamine yielded the 4-derivatives as the only readily isolable compounds.

Bromination of 2-ethoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine gave the 4-derivative as the main product accompanied by some 20% of the 6-derivative.



SCHEME B. *Orientation of bromo-compounds based on* (III) *and* (IV).

The results fall in line with the general observation that the products obtained on chlorination of an aromatic compound parallel those obtained on nitration, but bromination frequently follows a different course (V and VI are typical examples). A discordant observation is that of Wepster,[5] who has shown that *N*-toluene-*p*-sulphonyl-2 : 6-xylidine is nitrated at position 4, whereas, as is now shown, chlorination occurs at position 3 but bromination at position 4, the two monohalogen derivatives being in turn readily converted into the toluenesulphonamide (VII). Further, the acetamido-group in *N*-acetyl-2-methoxy-1-naphthylamine is perhaps not unsimilarly situated to that in 1-acetamido-2 : 6-xylidine and might be subjected to a similar suppression of resonance, if indeed such occurs.

[4] Consden and Kenyon, *J.*, 1935, 1593.
[5] Wepster, *Rec. Trav. chim.*, 1954, **73**, 814.

Experimental

Synthesis of N-*Acetyl*-3-*bromo*-2-*methoxy*-1-*naphthylamine.*—3-Bromo-1-nitro-2-naphthylamine [4] (5 g.) and a solution of sodium hydroxide (4 g.) in water (100 c.c.) were boiled under reflux for 6 hr. The filtered solution was acidified with hydrochloric acid, and the precipitate crystallised from a small bulk of ethanol to give 3-bromo-1-nitro-2-naphthol, yellow plates, m. p. 132° (without decomp.) (1·5 g.). From the mother-liquor was obtained material, m. p. *ca.* 180°, and this was boiled with benzene and then with chloroform to remove more soluble material. The residue on crystallisation from aqueous ethanol formed long, golden-yellow needles of 2 : 3-*dihydroxy*-1-*nitronaphthalene*, m. p. 210° (Found: C, 58·4; H, 3·1. $C_{10}H_7O_4N$ requires C, 58·5; H, 3·4%). 3-Bromo-1-nitro-2-naphthol can be purified by distillation in steam or by elution from alumina by ethyl acetate. It yielded a rather sparingly soluble sodium salt, which was not attacked by dimethyl sulphate. It was not methylated in xylene by dimethyl sulphate (K_2CO_3), but in ether with diazomethane methylation was smooth to give 3-*bromo*-2-*methoxy*-1-*nitronaphthalene*, which crystallised from methanol in silky, yellow needles, m. p. 83° (Found: C, 47·1; H, 3·0. $C_{11}H_8O_3NBr$ requires C, 46·8; H, 2·8%).

Stannous chloride (1 mol.) in concentrated hydrochloric acid was added to 3-bromo-2-methoxy-1-nitronaphthalene in boiling ethanol, and the solution concentrated. On being made alkaline with sodium hydroxide, the mixture rapidly became black and the base after extraction with ether and removal of the solvent was a black mass. It was dissolved in acetic anhydride and precipitated with water, and the dark, sticky product extracted with a small bulk of hot ethanol in order to remove most of the impurities. The residue, m. p. *ca.* 200°, was recrystallised first from acetic acid (charcoal) and then ethyl acetate to yield N-*acetyl*-3-*bromo*-2-*methoxy*-1-*naphthylamine* as a mass of fine needles, m. p. 210—213° (Found: C, 53·0; H, 4·1. $C_{13}H_{12}O_2NBr$ requires C, 53·1; H, 4·1%) (large depression with both 4-bromo- and the unoriented monobromo-isomer described below).

N-*Acetyl*-4-*bromo*-2-*methoxy*-1-*naphthylamine.*—*N*-Acetyl-4-amino-2-methoxy-1-naphthylamine [1] was diazotised in hydrobromic acid solution, and the filtered diazonium solution decomposed with copper powder. The precipitate was filtered off, and the *bromo-compound* removed from this by acetone. On recrystallisation from slightly aqueous acetic acid it formed needles, m. p. 211—213° (Found: C, 53·2; H, 4·0. $C_{13}H_{12}O_2NBr$ requires C, 53·1; H, 4·1%). A pure compound could not be isolated after treatment of this compound with bromine in acetic acid.

Bromination of N-*Acetyl*-2-*methoxy*-1-*naphthylamine.*—(*a*) Bromine (1 mol.) was added to a solution of the compound in chloroform, and the solution was then concentrated and diluted with light petroleum, and the resultant oil dissolved in acetic acid. The crop after further purification gave *N*-acetyl-6-bromo-2-methoxy-1-naphthylamine, m. p. 254°, in 20% yield.

(*b*) Addition of bromine (1 mol.) in acetic acid to the compound in warm acetic acid under various conditions gave highly impure products from which only the 6-bromo-derivative could be isolated in poor yield.

(*c*) After addition of *N*-bromosuccinimide (1 mol.) to a solution of the compound in pyridine the compound was recovered but in poor yield.

(*d*) Bromine (9 g.) in acetic acid (6 c.c.) was added to the compound (12 g.) in a mixture of acetic acid (60 c.c.) and acetic anhydride (6 c.c.) at room temperature. After a short time the mixture was heated to boiling and decomposed with a limited volume of water. The crop (7·8 g.) was essentially the 6-bromo-derivative with a small amount of the 4 : 6-dibromo-derivative (below). The filtrate on further dilution gave crystalline material, m. p. 180—197° (5·1 g.), which was separated by fractional crystallisation from acetic acid into the 4-bromo-derivative (above) and another *monobromo-derivative*, which formed prisms, m. p. 211—214° (Found: C, 54·1; H, 3·9%) greatly depressed on admixture with either the 3- or the 4-bromo-derivative. Chromium trioxide (2 g.) in the minimum of water was added to a hot solution of this compound (1 g.) in acetic acid (10 c.c.). The mixture was diluted with water, and the product recrystallised from acetic acid, to yield yellow needles of a *bromo*-2-*methoxy*-1 : 4-*naphthaquinone*, m. p. 190° (Found: C, 49·7; H, 2·8. $C_{11}H_7O_3Br$ requires C, 49·5; H, 2·6%), and an unidentified neutral compound, forming almost colourless plates, m. p. 176—178°.

Dr. D. M. W. Anderson, of Edinburgh University, has kindly provided the following report on the infrared spectra of the foregoing bromo-naphthalides:

" 3-Bromo: NH 3210; carbonyl 1665 vs, 1640 (sh), 1590 (all diffuse), 682 w, 728 m, 747 vs,

780 m, 805 w, 850 m cm.$^{-1}$. 4-Bromo: NH 3265; carbonyl 1660 vs, 1627 m, 1605 m (all sharp), 750 vs, 763 m, 793 w, 847 m, 900 m cm.$^{-1}$. 6-Bromo: NH 3260; carbonyl 1655 vs, 1635 (sh), 1596 m (all diffuse), 690 m, 800 vs, 815 vs, 880 vs, 900 m cm.$^{-1}$. (?)-Bromo: NH 3260 (broad); carbonyl 1660 (sh), 1650 vs (broad), 1622 m, 1603 m, 672 m, 755 m, 796 w, 830 vs, 937 m cm.$^{-1}$.

" Application of the principles of Cencelj and Hadži [6] and of Hawkins, Ward, and Whiffen [7] for substitution patterns leads to no precise conclusion regarding the structure of the last compound. The broad NH and carbonyl bands may indicate that these groups are involved in weak hydrogen-bonding effects and, if this is so, position 8 is indicated for the bromine."

Bromination of N-Acetyl-6-bromo-2-methoxy-1-naphthylamine.—Bromine (1 mol.) in acetic acid was added to a hot solution of the compound in acetic acid. On cooling, there separated a greenish deposit, which was washed with ammonia solution and then recrystallised from acetic acid to give the 4 : 6-*dibromo-derivative* as needles, m. p. 243° (Found: C, 42·6; H, 3·1. $C_{13}H_{11}O_2NBr_2$ requires C, 41·8; H, 3·0%). In appearance and solubility this compound closely resembles the 6-bromo-derivative, but the m. p. is depressed on admixture with it. It was recovered after treatment with ethanolic hydrogen chloride or potassium hydroxide. With hot 60% sulphuric acid it rapidly decomposed. Oxidation with chromium trioxide (as above) gave yellow needles, which suffered no depression in m. p. on admixture with 6-bromo-2-methoxy-1 : 4-naphthaquinone,[8] thereby establishing that the second bromine atom is in position 4.

Dr. D. M. W. Anderson had reported on the infrared spectrum of this compound: NH 3250; carbonyl 1663 vs, 1620 m, 1594 m (all sharp); 780, 815 vs, 838 m, 868 m, 903 s, 926 m, 978 s cm.$^{-1}$, and suggested that, owing to the striking similarity of the carbonyl region of this compound with that of the 4-isomer, the orientation would prove to be 4 : 6.

6-Bromo-2-ethoxy-N-formylnaphthylamine, prepared by boiling 6-bromo-2-ethoxy-1-naphthylamine with formic acid for 2 hr., crystallised from formic acid in needles, m. p. 229—231° (Found: C, 52·6; H, 3·9. $C_{13}H_{12}O_2NBr$ requires C, 53·1; H, 4·1%).

6-Bromo-2-ethoxy-N-toluene-p-sulphonyl-1-naphthylamine, prepared from the base and toluene-*p*-sulphonyl chloride in pyridine, crystallised from acetic acid in needles, m. p. 173° (Found: C, 54·7; H, 4·2. $C_{19}H_{18}O_3NSBr$ requires C, 54·3; H, 4·3%). Attempted further bromination either with *N*-bromosuccinimide in pyridine or with bromine in acetic acid led to dark, sticky products from which no definite compounds were isolated.

Bromination of 2-Ethoxy-N-formyl-1-naphthylamine.—Bromine (1 mol.) was added to a solution of the compound (2·9 g.) in warm chloroform. The very dark mixture was concentrated and diluted with light petroleum. A dark oil was precipitated which solidified (2·5 g.) when boiled with ethanol. After repeated recrystallisation from acetic acid or formic acid it gave *4-bromo-2-ethoxy-N-formyl-1-naphthylamine* as fine needles, m. p. 202—204° (Found: C, 53·3; H, 4·3. $C_{13}H_{12}O_2NBr$ requires C, 53·1; H, 4·1%). Hydrochloric acid (4 c.c.) was added to a suspension of this compound (1 g.) in boiling ethanol (16 c.c.). A clear solution was rapidly obtained which on slight concentration gave needles of the base hydrochloride. The liberated base (m. p. 85° without further purification) gave *N-acetyl-4-bromo-2-ethoxy-1-naphthylamine*, needles, m. p. 187°, from ethanol or acetic acid (Found: C, 54·6; H, 4·3. $C_{14}H_{14}O_2NBr$ requires C, 54·5; H, 4·5%), and *4-bromo-2-ethoxy-N-toluene-p-sulphonyl-1-naphthylamine*, rosettes, m. p. 149°, from acetic acid (Found: C, 53·8; H, 4·2. $C_{19}H_{18}O_3NSBr$ requires C, 54·3; H, 4·3%).

N-Acetyl-4-bromo-2-ethoxy-1-naphthylamine was alternatively prepared as follows. Sodium dithionite was added to a boiling suspension of *N*-acetyl-2-ethoxy-4-nitro-1-naphthylamine (2 g.) in water (20 c.c.) until the colour was discharged. The mixture was diluted with aqueous ammonia, and the product extracted with boiling ethanol. The amine, which separated in prisms, m. p. 197°, was diazotised in hydrobromic acid solution and decomposed with copper. The bromo-derivative was extracted from the product with a little acetone and purified by recrystallisation from acetic acid.

Bromination of N-Formyl-2-methoxy-1-naphthylamine.—The method employed for the ethoxy-analogue gave *4-bromo-1-formyl-2-methoxy-1-naphthylamine*, which crystallised from acetic acid in a cotton-wool-like mass of needles, m. p. 204° (Found: C, 51·9; H, 3·2.

[6] Cencelj and Hadži, *Spectrochim. Acta*, 1955, **7**, 274.
[7] Hawkins, Ward, and Whiffen, *ibid.*, 1957, **10**, 105.
[8] Bell, Gibson, and Wilson, *J.*, 1956, 2339.

$C_{12}H_{10}O_2NBr$ requires C, 51·4; H, 3·6%). This compound was very readily hydrolysed by ethanolic hydrochloric acid to *4-bromo-2-methoxy-1-naphthylamine*, which crystallised from methanol in plates, m. p. 68° (Found: C, 52·8; H, 3·8. $C_{11}H_{10}ONBr$ requires C, 52·4; H, 4·0%). This base with acetic anhydride gave an acetyl derivative, which underwent no depression in m. p. on admixture with synthetic *N*-acetyl-4-bromo-2-methoxy-1-naphthylamine, and with toluene-*p*-sulphonyl chloride gave a compound which underwent no change in m. p. on admixture with the compound [2] obtained by bromination of 2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine. The latter is therefore the 4-bromo-derivative.

2-Ethoxy-1-naphthylamine with toluene-*p*-sulphonyl chloride in pyridine gave the N-*toluene*-p-*sulphonyl derivative*, needles, m. p. 147°, from acetic acid (Found: N, 3·6. $C_{19}H_{19}O_3NS$ requires N, 4·1%).

Bromination of 2-*Ethoxy*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine.*—(*a*) Bromine (1 mol.) in chloroform was added to a warm suspension of the compound (3 g.) in chloroform (15 c.c.). The solution became very dark when boiled, and there was deposited a small amount of an unidentified hydrobromide (base, m. p. *ca.* 80°; acetyl derivative, m. p. 246—250°). The filtrate on dilution with light petroleum gave material which after repeated recrystallisation from acetic acid gave the 4-bromo-derivative, m. p. 149° (p. 522).

(*b*) *N*-Bromosuccinimide (1 mol.) was added to the compound in pyridine. The solution was decomposed by dilute hydrochloric acid to yield a dark oil, which was separated by decantation and dissolved in hot ethanol. The crop, after repeated recrystallisation, gave the 4-bromo-derivative.

(*c*) Bromine (1 mol.) in acetic acid was added to the compound (2 g.) in warm acetic acid (20 c.c.). After a short time the solution was poured into water, and the brown precipitate purified by crystallisation first from ethanol and then acetic acid. Both the 4-bromo- and the 6-bromo-derivative were isolated, the latter in about 20% yield after purification.

(*d*) Bromine (2 mol.) was used as in (*c*). On cooling, the mixture deposited crystals, m. p. *ca.* 190°, which after recrystallisation from acetic acid gave the *4 : 6-dibromo-derivative* as needles, m. p. 195—196° (Found: C, 46·3; H, 3·4. $C_{19}H_{17}O_3NSBr_2$ requires C, 45·7; H, 3·4%). This dibromo-derivative was readily obtained by bromination of both 4- and 6-bromo-2-ethoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamines.

Bromination of N-*Acetyl*-2-*ethoxy*-1-*naphthylamine.*—Addition of bromine (1 mol.) to a solution of the compound in chloroform or acetic acid–acetic anhydride (1 : 1) led to dark, complex mixtures from which by fractional crystallisation was isolated as the main product *N*-acetyl-6-bromo-2-ethoxy-1-naphthylamine, m. p. 252—254°, and a small amount of the 4-bromo-analogue (p. 522).

4-Chloro-2-methoxy-1-naphthylamine separated as the hydrochloride when *N*-acetyl-4-chloro-2-methoxy-1-naphthylamine [3] (2·5 g.) in ethanol (25 c.c.) was boiled with hydrochloric acid (10 c.c.). The hydrochloride was decomposed by aqueous ammonia to give the base, which crystallised from methanol in needles, m. p. 55° (Found: C, 63·6; H, 4·8. $C_{11}H_{10}ONCl$ requires C, 63·7; H, 4·8%), and with toluene-*p*-sulphonyl chloride in pyridine gave the *toluene-p-sulphonyl derivative*, needles (from acetic acid), m. p. 197° (Found: C, 59·3; H, 4·1. $C_{18}H_{16}O_3NSCl$ requires C, 59·7; H, 4·4%).

Chlorination of 2-*Methoxy*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine.*—The compound in warm acetic acid was treated with chlorine (1 mol.). The crop (m. p. *ca.* 190°) obtained on cooling was recrystallised from acetic acid to give the 4-chloro-derivative, m. p. 197° (above), in about 50% yield.

Chlorination of 2-*Ethoxy*-N-*toluene*-p-*sulphonyl*-1-*naphthylamine.*—The compound with sulphuryl chloride (1 mol.) in chloroform gave the *4-chloro-derivative*, which crystallised from acetic acid in needles, m. p. 147° (Found: C, 61·2; H, 4·4. $C_{19}H_{18}O_3NSCl$ requires C, 60·7; H, 4·8%).

Chlorination of N-*Acetyl*-2-*ethoxy*-1-*naphthylamine.*—Sulphuryl chloride (1 mol.) in chloroform was added dropwise to a solution of the compound in chloroform. The chloroform was removed on a steam-bath, and the dark residue taken up in hot ethanol. The crop, after several recrystallisations from ethanol, gave the *4-chloro-derivative* as needles, m. p. 177° (Found: C, 64·2; H, 5·0. $C_{14}H_{14}O_2NCl$ requires C, 63·8; H, 5·3%). A suitable method for the hydrolysis of this compound was not found.

N-*Acetyl*-2-*ethoxy*-4-*nitro*-1-*naphthylamine.*—Concentrated nitric acid (1·7 c.c.) was added dropwise to a cooled suspension of *N*-acetyl-2-ethoxy-1-naphthylamine (5 g.) in acetic acid

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(10 c.c.). After 2 hr., water was added, and the resulting plastic mass induced to solidify by rubbing it with warm ethanol. The product (1 g., m. p. 233—236°) gave the *4-nitro-derivative* as bright yellow needles, m. p. 234—236°, from acetic acid (Found: C, 61·5; H, 4·5. $C_{14}H_{14}O_4N_2$ requires C, 61·3; H, 5·1%). The yield was equally poor in other methods of nitration.

2-Ethoxy-4-nitro-1-naphthylamine.—This compound is mentioned in a patent [9] but no details of its preparation are given. 2-Ethoxy-*N*-formyl-1-naphthylamine (5 g.; m. p. 152°) was added slowly to a mixture of concentrated nitric acid (2·5 c.c.) and acetic acid (12·5 c.c.). After 2 hr. water was added to the pasty mass, and the product boiled with ethanol to yield the 4-nitro-derivative (2·5 g.), m. p. 211°. Potassium hydroxide (2 g. in a little water) was added to a boiling suspension of this nitro-compound (2·5 g.) in ethanol (50 c.c.). Hydrolysis was instantaneous. The clear solution was diluted with water, and on cooling 2-ethoxy-4-nitro-1-naphthylamine separated in bright red prisms, m. p. 152°. This base (1·5 g.) was left in pyridine with toluene-*p*-sulphonyl chloride (1·5 g.) for 24 hr., and the mixture then decomposed by excess of dilute hydrochloric acid. The sticky product was boiled successively with ethanol and ethyl acetate to remove unchanged base, and the residue recrystallised from acetic acid to give the *N-toluene-*p*-sulphonyl derivative* as yellow needles, m. p. 167—169° (Found: C, 59·6; H, 4·7. $C_{19}H_{18}O_5N_2S$ requires C, 59·1; H, 4·7%).

*Nitration of 2-Ethoxy-N-toluene-*p*-sulphonyl-1-naphthylamine.*—The compound (1 g.) was warmed on a steam-bath for about 2 hr. with a mixture of concentrated nitric acid (1 c.c.) and water (10 c.c.). The product on recrystallisation from acetic acid gave the pure 4-nitro-derivative (above).

The previously described [3] nitro-derivatives of *N*-formyl-2-methoxy- and 2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine were shown to be 4-nitro-derivatives in the following way. The formamido-4-nitro-compound was rapidly and almost quantitatively converted into 2-methoxy-4-nitro-1-naphthylamine by addition of a slight excess of concentrated aqueous potassium hydroxide to its solution in boiling ethanol. This base in pyridine with toluene-*p*-sulphonyl chloride was slowly and partially converted into the toluene-*p*-sulphonyl derivative, which was readily separated from the base by its much lower solubility in ethyl acetate. It formed yellow needles, m. p. 199° alone or mixed with the product of nitration of 2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine.

*Interaction of 2-Methoxy-N-toluene-*p*-sulphonyl-1-naphthylamine with Fuming Nitric Acid.*—Fuming nitric acid (2 c.c.) in acetic acid (2 c.c.) was added to a warm suspension of the compound (2 g.) in acetic acid (20 c.c.). Recrystallisation of the crystals from acetic acid gave *4-nitro-1 : 2-naphthaquinone 1-toluene-*p*-sulphonimide* in orange-red needles, m. p. 200° (decomp.) (Found: C, 57·6; H, 3·0. $C_{17}H_{12}O_5N_2S$ requires C, 57·3; H, 3·4%). The same compound was obtained by using either 2-ethoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine or 2-methoxy-4-nitro-*N*-toluene-*p*-sulphonyl-1-naphthylamine in the above experiment.

Oxidation of 2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine with chromic acid in acetic acid gave 2-methoxy-1 : 4-naphthaquinone,[1] m. p. 184°, in fair yield.

*4-Chloro-1 : 2-naphthaquinone 1-toluene-*p*-sulphonimide*, obtained from either 4-chloro-2-ethoxy- or 4-chloro-2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine by treatment with fuming nitric acid as above, formed bright red prisms, m. p. 220° (decomp.), from acetic acid (Found: C, 59·5; H, 3·5. $C_{17}H_{12}O_3NSCl$ requires C, 59·1; H, 3·5%) or long yellow needles from benzene.

6-Bromo-2-methoxy-*N*-toluene-*p*-sulphonyl-1-naphthylamine did not undergo smooth reaction with fuming nitric acid under the same conditions.

*Bromination of N-Toluene-*p*-sulphonyl-2 : 6-xylidine.*—*N*-Bromosuccinimide (1 mol.) was added to the compound in pyridine, and the resulting solution left for ½ hr. On decomposition with dilute hydrochloric acid the *4-bromo-derivative* was precipitated in almost theoretical yield. It formed needles, m. p. 149°, from acetic acid (Found: C, 50·7; H, 4·1. $C_{15}H_{16}O_2NSBr$ requires C, 50·9; H, 4·5%), and was hydrolysed during several days by concentrated sulphuric acid to give 4-bromo-2 : 6-xylidine, m. p. 47° (acetyl derivative, m. p. 195°). Bromination of *N*-toluene-*p*-sulphonyl-2 : 6-xylidine by bromine in chloroform gave a much less favourable result; the only solid product was 4-bromo-2 : 6-xylidine hydrobromide and most remained as an uncrystallisable oil.

[9] I. G. Farbenind., G.P. 491,022.

Chloro-*N*-toluene-*p*-sulphonyl-2 : 6-xylidine [10] was hydrolysed with concentrated sulphuric acid for several days to give an oily base which could not be solidified in ice and which gave an acetyl derivative, m. p. 146—147°. This agrees with 3-chloro-2 : 6-xylidine (liquid; acetyl derivative, m. p. 146—147°) and not 4-chloro-2 : 6-xylidine (m. p. 44—45°; acetyl derivative, m. p. 195°).[11]

4-Bromo-3-chloro-N-toluene-p-*sulphonyl-2 : 6-xylidine.*—(*a*) Excess of sulphuryl chloride was added to 4-bromo-*N*-toluene-*p*-sulphonyl-2 : 6-xylidine, and the excess removed on a steam-bath. The residual gum after repeated recrystallisation from acetic acid gave prisms identical with those obtained as below. (*b*) *N*-Bromosuccinimide (1 mol.) was added to 3-chloro-*N*-toluene-*p*-sulphonyl-2 : 6-xylidine dissolved in pyridine, and the mixture slightly warmed until solution resulted. Excess of dilute hydrochloric acid was added, and the precipitate recrystallised from acetic acid, giving *4-bromo-3-chloro-N-toluene*-p-*sulphonyl-2 : 6-xylidine* in prisms, m. p. 136° (Found: C, 46·8; H, 3·9. $C_{15}H_{15}O_2NSBrCl$ requires C, 46·3; H, 3·9%).

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[10] Bell, *J.*, 1955, 2382.
[11] Dadswell and Kenner, *J.*, 1927, 1105.

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109. *Pyrimidines. Part X.* Pyrimidine, 4 : 6-Dimethylpyrimidine, and their 1-Oxides.*

By R. R. HUNT, J. F. W. MCOMIE, and E. R. SAYER.

A convenient four-stage synthesis of pyrimidine is described which starts from acetylacetone and thiourea, and proceeds *via* 2-mercapto-4 : 6-dimethylpyrimidine, 4 : 6-dimethylpyrimidine, and pyrimidine-4 : 6-dicarboxylic acid.

Other syntheses of pyrimidine and of 4-methylpyrimidine have been explored. Pyrimidine and its 4 : 6-dimethyl derivative, when treated with hydrogen peroxide in acetic acid, give the corresponding 1-oxides, but these could only be made to undergo two of the many rearrangements typical of the pyridine 1-oxides.

As a prelude to studies of substitution in pyrimidine we have devised a convenient, four-stage synthesis of this compound in which the usual tedious isolation *via* the mercuric chloride complex has been avoided. Acetylacetone reacts with thiourea to give 2-mercapto-4 : 6-dimethylpyrimidine which is desulphurised to give 4 : 6-dimethylpyrimidine. Oxidation of the latter to pyrimidine-4 : 6-dicarboxylic acid followed by pyrolysis then gives pyrimidine. The sequence has not previously been used for the preparation of pyrimidine, yet each of the four reactions has been effected at various times, although no details of the last two stages have been published.

The condensation of acetylacetone with thiourea by Evans's method [1] gave a mixture of 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride and a 1 : 1 molecular complex [2] of the pyrimidine with thiourea, but by modifying the conditions a 90% yield of the pyrimidine hydrochloride, free from thiourea, was obtained. Desulphurisation of the mercapto-compound by Raney nickel was first studied in neutral aqueous solution. At the end of the reaction the mixture was filtered and steam-distilled until the distillate no longer gave a turbidity with mercuric chloride. The distillate then contained 4 : 6-dimethylpyrimidine in 68—72% yield, but when attempts were made to oxidise the dimethylpyrimidine in this solution much more than the theoretical amount of potassium

* Part IX, *J.*, 1957, 1830.

[1] Evans, *J. prakt. Chem.*, 1893, **48**, 493.
[2] Boarland and McOmie, *J.*, 1952, 3722.

permanganate was consumed and the yield of pyrimidine-4 : 6-dicarboxylic acid was low. Presumably some di- or tetra-hydro-4 : 6-dimethylpyrimidine had been produced and complete oxidation of this would account for the large amount of potassium permanganate required. The desulphurisation was therefore carried out in ethanol, and the 4 : 6-dimethylpyrimidine (45—60% yield) isolated by distillation. The yield was not improved by converting the mercaptopyrimidine into 4 : 6-dimethyl-2-methylthiopyrimidine before desulphurisation.

Oxidation of 4 : 6-dimethylpyrimidine by alkaline potassium permanganate gave good but variable (43—72%) yields of pyrimidine-4 : 6-dicarboxylic acid. A less favourable conversion was effected by bromination of the dimethylpyrimidine followed by hydrolysis of the 4 : 6-bistribromomethylpyrimidine with silver nitrate in acetic acid. Similar conversions have been carried out by Brown *et al.*[3] in the pyrimidine and quinoline series and by Holland and Slack [4] for the preparation of 5-bromopyrimidine-2-carboxylic acid. The dicarboxylic acid could be decarboxylated on a very small scale by dry distillation,[5] but even on a one-gram scale the yield dropped so much that the method was useless. However, by heating the acid in diphenyl ether, it was possible to decarboxylate 38-gram batches in 60% yield. Thus pyrimidine is available in an overall yield of 10—23% based on acetylacetone.

The commercial availability of 1 : 1 : 3 : 3-tetraethoxypropane suggested the possibility of a two-stage synthesis of pyrimidine. Thiourea and the acetal in presence of hydrochloric acid readily gave 2-mercaptopyrimidine, but re-investigation of the desulphurisation of the latter [6] showed that the yield of pyrimidine was unsatisfactory, even if the 2-mercapto-compound was first converted into 2-methylthiopyrimidine or 2-(pyrimidylthio)acetic acid. Oxidative desulphurisation of 2-mercaptopyrimidine by the method of Evans *et al.*[7] was more promising but large-scale experiments were not carried out. 1 : 1 : 3 : 3-Tetraethoxypropane also condensed readily with urea to give 2-hydroxypyrimidine, but it could not be condensed with benzamidine. Bredereck, Gompper, and Morlock [8] recently showed that 1 : 1 : 3-triethoxy-3-methoxypropane and formamide gave pyrimidine in 65% yield, so that this method is the simplest so far devised. We have shown that 1 : 1 : 3 : 3-tetraethoxypropane also undergoes this reaction, but we obtained only a 30% yield of pyrimidine. A few experiments were made to utilise the commercially available 1-methoxybut-1-en-3-yne. Condensation with thiourea in presence of hydrochloric acid gave 2-mercapto-4-methylpyrimidine hydrochloride which on desulphurisation with Raney nickel gave a low yield of 4-methylpyrimidine.

Pyridine 1-oxide and related compounds undergo a variety of substitution and rearrangement reactions (for reviews see Ochiai [9] and Katritzky [10]). Ochiai [9,11] prepared the *N*-oxides of a few substituted pyrimidines and showed that with alkali-metal cyanides in the presence of benzoyl chloride they give cyanopyrimidines. After completion of our work, Wiley and Slaymaker [12] described the preparation of the *N*-oxides of pyrimidine and the monoethyl- and 2 : 4 : 6-trimethyl-pyrimidines. Employing the usual method of oxidation with hydrogen peroxide in acetic acid we found that 4 : 6-dimethylpyrimidine 1-oxide could be obtained easily but pyrimidine itself gave only a 9% yield of oxide (Wiley and Slaymaker [12] obtained an 11% yield under slightly different conditions). The following 4 : 6-dimethylpyrimidines gave no *N*-oxides, possibly because of steric hindrance: 2-benzyloxy-, 2-chloro-, 2-hydroxy-, and 2-phenyl-.

[3] Brown, Hammick, and Thewlis, *J.*, 1951, 1146.
[4] Holland and Slack, *Chem. and Ind.*, 1954, 1203.
[5] Angerstein, *Ber.*, 1901, **34**, 3956.
[6] Boarland, McOmie, and Timms, *J.*, 1952, 4691.
[7] Evans, Jones, Palmer, and Stephens, *J.*, 1956, 4106.
[8] Bredereck, Gompper, and Morlock, *Chem. Ber.*, 1957, **90**, 942.
[9] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[10] Katritzky, *Quart. Rev.*, 1956, **10**, 395.
[11] Ochiai and Yamanaka, *Pharm. Bull.* (*Japan*), 1955, **3**, 175.
[12] Wiley and Slaymaker, *J. Amer. Chem. Soc.*, 1957, **79**, 2233.

4 : 6-Dimethylpyrimidine 1-oxide and toluene-*p*-sulphonyl chloride gave a low yield of a very unstable chlorine-containing product, not identical with 2-chloro-4 : 6-dimethylpyrimidine. The product is considered to be 4-chloromethyl-6-methylpyrimidine since the other possible product, 5-chloro-4 : 6-dimethylpyrimidine, would be expected to be stable; moreover, 2-methylpyridine 1-oxide is known to give 2-chloromethylpyridine in this reaction.[13] When 4 : 6-dimethylpyrimidine 1-oxide was heated in acetic anhydride it gave what is thought to be 4-acetoxymethyl-6-methylpyrimidine—by analogy with the pyridine series,[14] and because the absorption spectrum ($\lambda_{max.}$ 248 mμ, $\log_{10}\varepsilon$ 3·48) of the product in ethanol closely resembles that of 4 : 6-dimethylpyrimidine (245·5 mμ, $\log_{10}\varepsilon$ 3·30).

Attempts to nitrate pyrimidine 1-oxide were unsuccessful and no useful products were obtained by the reaction of 4 : 6-dimethylpyrimidine 1-oxide under the conditions used in the pyridine and quinoline series with phenylmagnesium bromide,[15] benzoyl chloride–potassium hydroxide,[16] or benzoyl chloride–potassium cyanide.[16] It is clear that the pyrimidine 1-oxides are much less useful for synthetic purposes than the pyridine or quinoline oxides.

The ultraviolet absorption spectra of some of the compounds described in this paper have been measured. It is known[17] that the spectrum of pyrimidine ($\lambda_{max.}$ 243 mμ, $\log_{10}\varepsilon$ 3·38) and of 4 : 6-dimethylpyrimidine ($\lambda_{max.}$ 246 mμ, $\log_{10}\varepsilon$ 3·63) in water is scarcely altered when the bases are converted into their hydrochlorides. Like the latter the 1-oxides bear a positive charge on one of the nitrogen atoms, but the spectrum of pyrimidine 1-oxide ($\lambda_{max.}$ 258 mμ, $\log_{10}\varepsilon$ 4·00) and that of 4 : 6-dimethylpyrimidine 1-oxide ($\lambda_{max.}$ 257 mμ, $\log_{10}\varepsilon$ 4·02) show a bathochromic displacement. For comparison, the methiodides of pyrimidine and of 4 : 6-dimethylpyrimidine in water were also examined. They absorbed at 226, 293 mμ ($\log_{10}\varepsilon$ 4·21, 3·18) and 226, 247 (infl.) mμ ($\log_{10}\varepsilon$ 4·18, 3·86) respectively. The short-wavelength band is probably due to the iodide anion which absorbs at 226 mμ ($\log_{10}\varepsilon$ *ca.* 4) in water, the absorption being due to charge transfer from the ion to the solvent.[18] The long-wavelength band is probably due to charge transfer from the iodide ion to the 1-methylpyrimidinium cation, and is similar to that discussed by Kosower[19] for pyridine methiodide.

Experimental

2-Mercapto-4 : 6-dimethylpyrimidine.—Concentrated hydrochloric acid (250 ml.) was added to a suspension of finely powdered thiourea (76 g., 1 mole) in acetylacetone (120 g., 1·2 moles) and ethanol (2500 ml.), and the mixture boiled under reflux for 2 hr. After cooling, the yellow needles (140 g., 80%) of 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride were collected. To the mother-liquor were added more powdered thiourea (76 g.), acetylacetone (110 g.), ethanol (100 ml.), and concentrated hydrochloric acid (150 ml.), and the mixture was boiled as before. Cooling and filtration then gave the hydrochloride (160 g., 90%). After three such preparations making use of the original mother-liquor, the final mother-liquor was discarded. The batches of hydrochloride gave a white precipitate with ammoniacal silver nitrate and were sufficiently pure to be used in the next stage. When the hydrochloride was contaminated with thiourea a brown precipitate was obtained.

4 : 6-Dimethylpyrimidine.—(*a*) Raney nickel[20] (180 g., ethanol-wet), followed by concentrated hydrochloric acid (30 ml.), was added to 2-mercapto-4 : 6-dimethylpyrimidine hydrochloride (90 g.) in ethanol (600 ml.) at *ca.* 50°. The mixture was boiled under reflux for 4 hr. while being stirred. The hot solution was filtered, the nickel was washed with hot ethanol (75 ml.), and the combined filtrates were concentrated to *ca.* 150 ml. This solution was mixed with ether (150 ml.) and then transferred to a large mortar. Powdered sodium hydroxide was

[13] Matsumura, *J. Chem. Soc. Japan*, 1953, **74**, 363.
[14] Boekelheide and Linn, *J. Amer. Chem. Soc.*, 1954, **76**, 1286.
[15] Colonna and Risaliti, *Gazzetta*, 1953, **83**, 58.
[16] Montanari and Pentimalli, *ibid.*, p. 273.
[17] Boarland and McOmie, *J.*, 1951, 1218.
[18] Smith and Symons, *Trans. Faraday Soc.*, 1958, **54**, 338.
[19] Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3253.
[20] Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 353.

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added in portions and ground into the sludge (much heat evolved) until the mixture was strongly alkaline. The liquid was decanted and the solid ground with more ether until about 500 ml. of extract had been obtained. After being filtered (sintered-glass funnel) and dried, the ethereal solution was distilled. The fraction of b. p. 45—110° was mainly ethanol and was used as part of the solvent for another desulphurisation, thereby raising the yield of dimethylpyrimidine by 5—8%. The fraction boiling above 110° was collected and redistilled through a short fractionating column, giving dimethylpyrimidine (25—30 g., 45—55%), b. p. 154°/758 mm., m. p. 24—26° (lit.,[21] 25°) [picrate, m. p. 143° (lit.,[21] 143°)]. The *methiodide* recrystallised from ethanol as needles, m. p. 220—222° (decomp.) (Found: C, 34·1; H, 4·3; N, 11·5. $C_7H_{11}N_2I$ requires C, 33·7; H, 4·4; N, 11·2%).

(*b*) The mercaptopyrimidine in aqueous sodium hydrogen carbonate was treated with methyl sulphate, yielding 4 : 6-dimethyl-2-methylthiopyrimidine as a light yellow oil (61%), b. p. 123—126°/15 mm., m. p. 21—24° (lit.,[22] b. p. 123—125°/14 mm., m. p. 23—24°). A mixture of the methylthio-compound (4·6 g.) and Raney nickel (22 g.) in water (38 ml.) and ethanol (12 ml.) was boiled under reflux for 2 hr. After being filtered, the solution was steam-distilled and a saturated aqueous solution of mercuric chloride added to the distillate, giving the adduct with 4 : 6-dimethylpyrimidine ($C_6H_8N_2,2HgCl_2$; 15 g., 77%).

Pyrimidine-4 : 6-dicarboxylic Acid.—A hot solution of potassium permanganate (90 g.) in water (550 ml.) was added during ~3 hr. to a stirred solution of 4 : 6-dimethylpyrimidine (15 g.) in water (50 ml.) containing sodium hydroxide (3·6 g.), at 70—80°. The hot solution was filtered and the manganese dioxide washed with hot water (50 ml.). The filtrate and washings were concentrated to *ca.* 100 ml., and concentrated hydrochloric acid was added until the pH was 2—3. After cooling, pyrimidine-4 : 6-dicarboxylic acid dihydrate, m. p. 210—211° (decomp.), was collected. In 25 oxidations the yield varied from 43 to 72% (average 60%).

Pyrimidine.—(*a*) Pyrimidine-4 : 6-dicarboxylic acid dihydrate (46 g.) was dried at 60° for one week to give the anhydrous acid (38 g.), m. p. 218° (decomp.) [lit.,[5] m. p. 220—222° decomp.)].

Anhydrous pyrimidine-4 : 6-dicarboxylic acid (38 g.) was added in portions to dry, redistilled diphenyl ether (50 g.) in a two-necked flask heated in an oil-bath at about 240° and fitted with a still-head, condenser, and receiver. Decarboxylation was rapid and, by maintaining the pressure in the system at a few mm. below atmospheric, the pyrimidine formed distilled over rapidly together with some diphenyl ether. When the decarboxylation was complete the distillate was redistilled through a short fractionating column, giving pyrimidine (10·7 g., 60%), b. p. 124—128°/760 mm.

(*b*) 2-Mercaptopyrimidine (0·5 g.) was desulphurised as previously described,[6] and the pyrimidine obtained was isolated as its complex with mercuric chloride (0·38 g., 25%), m. p. 230—232° (Found: C, 14·1; H, 1·3; N, 8·2. Calc. for $C_4H_4N_2,HgCl_2$: C, 13·7; H, 1·1; N, 8·0%).

(*c*) A mixture of 2-(pyrimidylthio)acetic acid (0·34 g.) (see below), sodium carbonate (0·15 g.), and ethanol-wet Raney nickel (1·6 g.) in ethanol (10 ml.) was boiled under reflux for 2 hr. After filtration the solution was distilled and a saturated ethanol solution of picric acid was then added to the distillate, giving pyrimidine picrate (0·086 g., 14%), m. p. 150—155°.

(*d*) 6% Hydrogen peroxide (15 ml.) was added dropwise during 1 hr. to an ice-cold solution of 2 mercaptopyrimidine (2 g.) in 2N-sodium hydroxide. After being stirred for 1·5 hr. more, the solution was made slightly acid by the addition of acetic acid. 2-Mercaptopyrimidine (0·3 g.) was removed and the filtrate was then concentrated to dryness under reduced pressure. Concentrated hydrochloric acid was added to the residue, whereupon sulphur dioxide was evolved. Sodium carbonate solution was added until the mixture was alkaline, then it was continuously extracted with ether for 2 hr. The ether reservoir contained picric acid, thus converting the extracted pyrimidine into its picrate which was collected (2·15 g., 39%; m. p. 152—155°).

4 : 6-*Bistribromomethylpyrimidine.*—Bromine (52 g.) in glacial acetic acid (48 ml.) was added dropwise during 2 hr. to a well-stirred mixture of anhydrous sodium acetate (30 g.) and 4 : 6-dimethylpyrimidine (5·4 g.) in acetic acid (48 ml.) and acetic anhydride (10 ml.) at 70—80°. After a further 5 hours' heating at 80—85° the acetic acid and excess of bromine were removed by distillation and the residue was poured into ice-water. The crude product (25 g.) was

[21] Gabriel and Colman, *Ber.*, 1899, **32**, 1536.
[22] Wheeler and Jamieson, *Amer. Chem. J.*, 1904, **32**, 342.

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recrystallised from light petroleum (b. p. 60—80°), giving orange needles (12·5 g.), m. p. 118—121°. A second recrystallisation then gave 4 : 6 *bistribromomethylpyrimidine* as pale fawn needles (11·2 g., 39%), m. p. 125—126° (Found: C, 12·4; H, 0·2; N, 4·9; Br, 81·5. $C_6H_2N_2Br_6$ requires C, 12·4; H, 0·4; N, 4·8; Br, 82·4%), $\lambda_{max.}$ 267 mμ ($\log_{10}$ ε 3·89) in ethanol.

Hydrolysis of 4 : 6-*Bistribromomethylpyrimidine.*—4 : 6-Bistribromomethylpyrimidine (2·9 g.) was boiled under reflux for 3 hr. with silver nitrate (4·6 g.) in acetic acid (40 ml.). The hot mixture was filtered and, after cooling, the filtrate gave pyrimidine-4 : 6-dicarboxylic acid (0·2 g., 24%), m. p. and mixed m. p. 206° (decomp.).

Methyl Pyrimidine-4 : 6-*dicarboxylate.*—A solution of the hydrated dicarboxylic acid (1·3 g.) in methanol (150 ml.) containing concentrated hydrochloric acid (1 ml.) was boiled under reflux for 0·5 hr. The solvent was removed under reduced pressure, and the residue was recrystallised from light petroleum (b. p. 60—80°), giving needles (1·0 g., 80%), m. p. 77—79°, which after sublimation had m. p. 82—83° (Found: C, 49·1; H, 4·3; OMe, 30·7. $C_8H_8O_4N_2$ requires C, 49·0; H, 4·1; N, 14·3; OMe, 32·6%), $\lambda_{max.}$ 269, 320 mμ ($\log_{10}$ ε 3·80, 2·46) in ethanol.

2-*Mercaptopyrimidine.*—1 : 1 : 3 : 3-Tetraethoxypropane (11 g.) was added to a hot, stirred mixture of thiourea (3·8 g.), ethanol (30 ml.), and concentrated hydrochloric acid (9 ml.). After being boiled for 10 min., the mixture was cooled and the yellow 2-mercaptopyrimidine (3·0 g.) collected. Addition of ether to the filtrate gave a further quantity (0·8 g.; total, 66%). Recrystallisation from ethanol–water gave the pure compound, m. p. 229—230° (decomp.) [lit.,[17] m. p. 230° (decomp.)] (Found: C, 43·0; H, 3·9; N, 24·9. Calc. for $C_4H_4N_2S$: C, 42·9; H, 3·6; N, 25·0%).

2-(*Pyrimidylthio*)*acetic Acid.*—A mixture of 2-mercaptopyrimidine (2 g.) and chloroacetic acid (1·5 g.) in water (10 ml.) was boiled under reflux for 0·5 hr. On cooling, the solution yielded 2-(*pyrimidylthio*)*acetic acid* (1·8 g., 60%), m. p. 190—197° raised to 199—200° by recrystallisation from water (Found: C, 42·2; H, 3·8; N, 16·6. $C_6H_6O_2N_2S$ requires C, 42·4; H, 3·5; N, 16·5%).

2-*Hydroxypyrimidine.*—1 : 1 : 3 : 3-Tetraethoxypropane (5·5 g.) was added to a warm solution of urea (1·5 g.) in ethanol (10 ml.) and concentrated hydrochloric acid (5 ml.). After being stirred at 30—40° for 1 hr., the solution was cooled to 0° and the 2-hydroxypyrimidine hydrochloride (1·3 g.), m. p. 210°, was collected. Addition of ether to the mother-liquor gave a further crop (1·2 g.) of the hydrochloride. The combined product was dissolved in aqueous sodium carbonate, then acidified to pH 5 with 5N-sulphuric acid. The solution was evaporated to dryness and the residue, after being powdered, was extracted with boiling ethyl acetate (1500 ml.). The extract gave 2-hydroxypyrimidine (1·8 g., overall yield 73%) as needles, m. p. and mixed m. p. 179—181°.

2-*Mercapto*-4-*methylpyrimidine Hydrochloride.*—Concentrated hydrochloric acid (62 ml.) and 1-methoxybut-1-en-3-yne (29 g.) were added to a solution of thiourea (25·5 g.) in ethanol (275 ml.), and the mixture was boiled under reflux for 6 hr. Next day the yellow-brown precipitate (43·8 g.) of 2-mercapto-4-methylpyrimidine hydrochloride was collected. Concentration of the filtrate gave a further amount (2·8 g.) of the hydrochloride. In agreement with Burness,[23] attempts to recrystallise the compound resulted in an insoluble polymer.

The crude mercaptopyrimidine, dissolved in aqueous sodium hydrogen carbonate, was treated with methyl sulphate, giving 4-methyl-2-methylthiopyrimidine (60%), b. p. 116—119°/21 mm., which gave a picrate, m. p. 108—110° (lit.,[24] m. p. 106—108°).

4-*Methyl*-2-(*pyrimidylthio*)*acetic Acid.*—A mixture of 2-mercapto-4-methylpyrimidine hydrochloride (1·6 g.) and sodium hydroxide (1·2 g.) in water (10 ml.) was added to a solution of chloroacetic acid (1 g.) in water (3 ml.) previously neutralised with sodium carbonate. After 4 days the mixture was acidified with dilute hydrochloric acid. The pale brown powder obtained recrystallised from water, giving 4-*methyl*-2-(*pyrimidylthio*)*acetic acid* as plates (0·75 g., 41%), m. p. 191° (Found: N, 15·0. $C_7H_8O_2N_2S$ requires N, 15·2%).

4-*Methylpyrimidine.*—Water-wet Raney nickel (20 g.) was added to a solution of 2-mercapto-4-methylpyrimidine hydrochloride (8 g.) in water (75 ml.) which had been neutralised by adding sodium carbonate. The mixture was boiled under reflux, with stirring, for 3 hr., then filtered hot, and the filtrate distilled. Ether-extraction of the distillate gave 4-methylpyrimidine (0·9 g., 20%), b. p. 139—140°/763 mm. The adduct with mercuric chloride had m. p. 198—200° (lit.,[21] m. p. 198°), and the picrate had m. p. 130—131° (lit.,[21] 131—134°).

[23] Burness, *J. Org. Chem.*, 1956, **21**, 97.
[24] Marshall and Walker, *J.*, 1951, 1013.

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4 : 6-*Dimethylpyrimidine* 1-*Oxide*.—A mixture of **4 : 6**-dimethylpyrimidine (10·8 g.), acetic acid (60 ml.), and 30% hydrogen peroxide (10 ml.) was kept at 70—80° for 3 hr., then more hydrogen peroxide (8 ml.) was added and the mixture warmed for 9 hr. more. Most of the solvent was removed under reduced pressure, then a little water was added, and the mixture again distilled. Anhydrous potassium carbonate was added to the residue until it was strongly alkaline. The resulting pasty mass was extracted in a Soxhlet apparatus with chloroform (100 ml.) for 3 hr. The chloroform solution, after being dried, was concentrated to *ca.* 15 ml., and light petroleum (b. p. 40—60°) added, precipitating **4 : 6-*dimethylpyrimidine* 1-*oxide*** (7·1 g., 57%), m. p. 100—102°. After two recrystallisations the compound was obtained as hygroscopic needles, m. p. 113—115° (Found: C, 58·2; H, 6·3; N, 22·2. $C_6H_8ON_2$ requires C, 58·0; H, 6·4; N, 22·6%). The oxide was without action on acidified starch–iodide paper. It gave a ***picrate***, m. p. 86° (from ethanol) (Found: C, 41·0; H, 3·2; N, 20·1. $C_{12}H_{11}O_8N_5$ requires C, 40·9; H, 3·1; N, 19·8%). The ***mercuric chloride adduct*** had, after recrystallisation from water, m. p. 158° [Found: C, 13·7; H, 1·5; N, 5·6. $(C_6H_8ON_2)_2(HgCl_2)_3$ requires C, 13·5; H, 1·5; N, 5·3%].

4-*Chloromethyl*-6-*methylpyrimidine*.—A mixture of **4 : 6**-dimethylpyrimidine 1-oxide (3·3 g.) and toluene-*p*-sulphonyl chloride (5·0 g.) in benzene (20 ml.) was kept at room temperature for 0·5 hr. The benzene was distilled off under reduced pressure and the residual oil heated on a water-bath for 1 hr. After being cooled, the oil was washed with ether, then aqueous sodium hydrogen carbonate was added and the mixture extracted with chloroform. The extract was distilled under a high vacuum and gave a very unstable chlorine-containing yellow oil which was immediately treated with picric acid in ethanol, giving **4-*chloromethyl*-6-*methylpyrimidine* *picrate***, m. p. 115° (Found: C, 38·8; H, 2·7; N, 18·1. $C_{12}H_{10}O_7N_5Cl$ requires C, 38·8; H, 2·7; N, 18·8%).

4-*Acetoxymethyl*-6-*methylpyrimidine*.—Acetic anhydride (10 ml.) was added to **4 : 6**-dimethylpyrimidine 1-oxide (2·5 g.) and after 10 min. the mixture was heated on the water-bath for 15 min. A vigorous exothermic reaction occurred and the liquid became almost black. The mixture was distilled and the pale yellow fraction (0·9 g.) of b. p. 130—150°/0·1 mm. was twice redistilled, giving **4-*acetoxymethyl*-6-*methylpyrimidine*** as a colourless oil, b. p. 100—110° (bath temp.)/15 mm. (Found: C, 57·0; H, 6·0; N, 16·5. $C_8H_{10}O_2N_2$ requires C, 57·6; H, 6·0; N, 16·9%). This gave a ***picrate*** which after two recrystallisations from ethanol formed yellow needles, m. p. 135—136° (Found: C, 42·9; H, 3·2. $C_{14}H_{13}O_9N_5$ requires C, 42·7; H, 3·3%).

Pyrimidine* 1-*Oxide*.**—A mixture of pyrimidine (6 g.), glacial acetic acid (45 ml.), and 36% hydrogen peroxide (7·5 ml.) was kept at 70—80° for 3 hr., then more hydrogen peroxide (6 ml.) was added and the mixture warmed for 9 hr. more. Acetic acid was removed under reduced pressure and sodium carbonate was added to the residue until the mixture became alkaline; then it was continuously extracted with chloroform, yielding brown needles (1·1 g.) which were purified by sublimation followed by recrystallisation from light petroleum (b. p. 40—60°)–benzene. The oxide (0·6 g., 9%) formed very deliquescent white needles, m. p. 89—91° (lit.,[12] m. p. 85—88°) which became brown after a few days (Found: C, 50·0; H, 4·1; N, 29·4. Calc. for $C_4H_4ON_2$: C, 50·0; H, 4·2; N, 29·2%). The oxide formed a ***picrate, m. p. 84—85° (Found: C, 37·0; H, 2·3. $C_{10}H_7O_8N_5$ requires C, 37·0; H, 2·2%), and a mercuric chloride adduct, m. p. 161—162°.

2-*Benzyloxy*-4 : 6-*dimethylpyrimidine*. 2-Chloro-4 : 6-dimethylpyrimidine (15 g.) was added to a solution of sodium (2·5 g.) in benzyl alcohol (75 ml.), and the mixture boiled under reflux for 4 hr., cooled, and poured into water. The product was extracted with ether, giving an oil, b. p. 188—195°/20 mm., which was redistilled, giving **2-*benzyloxy*-4 : 6-*dimethylpyrimidine*** (14·7 g.), b. p. 160—165°/2·5 mm. (Found: C, 72·8; H, 6·4; N, 13·1. $C_{13}H_{14}ON_2$ requires C, 73·0; H, 6·6; N, 13·2%).

The 2-benzyloxy-compound (2 g.) was easily debenzylated by boiling 20% hydrochloric acid (10 ml.) (20 min.). After cooling, the mixture was made neutral and extracted with chloroform, which on evaporation gave 2-hydroxy-4 : 6-dimethylpyrimidine dihydrate (0·9 g., 60%), m. p. 198°.

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THE UNIVERSITY, BRISTOL. [*Received, October 3rd*, 1958.]

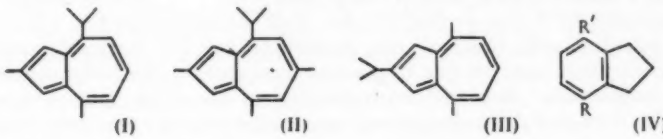
110. *The Structure of Zierone. Part. I. The Synthesis of Zierazulene and 6-Methylzierazulene.*

By D. J. Collins.

2 : 4-Dimethyl-8-*iso*propyl- (I) and 2 : 4 : 6-trimethyl-8-*iso*propyl-azulene (II) have been synthesised and shown to be identical with respectively zierazulene and a methyl derivative thereof.

In a preliminary communication [1] it was stated that reduction and dehydrogenation of the sesquiterpene ketone zierone, $C_{15}H_{22}O$, gave a new violet azulene, zierazulene, $C_{15}H_{18}$. Similarly, by reduction and dehydrogenation of hydroxymethylenezierone, $C_{16}H_{22}O_2$, was obtained a new tetra-alkylazulene, $C_{16}H_{20}$, in which the alkyl group was in a position next to that previously occupied by the keto-group. On the basis of visible spectra, the isoprene rule, and other chemical evidence,[2] the structures (I) and (II) were assigned to zierazulene and the methyl derivative, respectively. The synthesis of 2 : 4-dimethyl-8-*iso*propyl- (I) and 2 : 4 : 6-trimethyl-8-*iso*propyl-azulene (II) has confirmed these deductions.

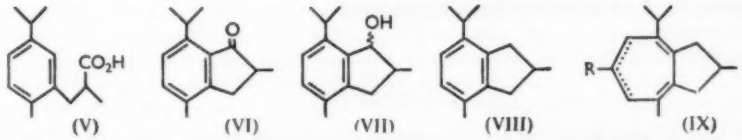
The diazoacetic ester–indane ring-expansion, used by Pfau and Plattner [3] in their synthesis of vetivazulene (III), is often ambiguous with 5- or 6-substituted indanes (cf., *e.g.*, the synthesis of S-guaiazulene, in which 1 : 4-dimethyl-6-*iso*propylazulene was also formed [4]). With indan (IV) substituted in the 4- or the 4 : 7-positions, this difficulty



(I) (II) (III) (IV)

does not arise. 4 : 8-Disubstituted azulenes synthesised by this method include 2 : 4 : 8-trimethyl-,[5] 1 : 4 : 8-trimethyl-,[6] and 1 : 4-dimethyl-8-*iso*propyl-azulene.[6]

Chloromethylation of *p*-cymene gave 2-chloromethyl-*p*-cymene,[7,8] which on condensation with ethyl methylmalonate, followed by hydrolysis and decarboxylation, gave α-methyl-β-(2-methyl-5-*iso*propylphenyl)propionic acid [7,9] (V). Friedel–Crafts cyclisation of the derived acid chloride gave 2 : 4-dimethyl-7-*iso*propylindan-1-one (VI), which was reduced by lithium aluminium hydride to the *cis-trans*-isomeric indanols (VII). Clemmen-



(V) (VI) (VII) (VIII) (IX)

sen reduction of the ketone (VI) afforded the indane (VIII). Treatment of the latter with diazoacetic ester in the usual way, and hydrolysis of the crude ester (IX; R = CO_2Et) obtained, gave the acid which with 10% palladium–charcoal at 250° underwent decarboxylation and dehydrogenation to 2 : 4-dimethyl-8-*iso*propylazulene (I). This hydrocarbon

[1] Birch, Collins, and Penfold, *Chem. and Ind.*, 1955, 1773.
[2] Unpublished work.
[3] Pfau and Plattner, *Helv. Chim. Acta*, 1939, **22**, 202.
[4] Plattner, Fürst, Marti, and Schmid, *ibid.*, 1949, **32**, 2137; Plattner, Fürst, and Marti, *ibid.*, p. 2452.
[5] Herz, *J. Amer. Chem. Soc.*, 1951, **73**, 4923.
[6] Herz, *ibid.*, 1952, **74**, 1350.
[7] Whittleston, *ibid.*, 1937, **59**, 825.
[8] Kadesch, *ibid.*, 1944, **66**, 1207.
[9] Rapson and Short, *J.*, 1933, 128.

was isolated by chromatography on alumina, purified by several successive extractions into syrupy phosphoric acid, and converted into its *s*-trinitrobenzene complex which after two recrystallisations from ethanol melted at 120°. The azulene was recovered by chromatography on alumina, again subjected to the phosphoric acid extraction procedure, and reconverted into its *s*-trinitrobenzene adduct which now melted at 122·5°, and did not depress the melting point of the corresponding zierazulene adduct. Likewise, the two picrates showed no depression of melting point. The visible spectrum of 2 : 4-dimethyl-8-*iso*propylazulene showed $\lambda_{max.}$ 545 mμ, $\lambda_{infl.}$ 582, 632 mμ, and is virtually identical with that of zierazulene [1] ($\lambda_{max.}$ 546 mμ, $\lambda_{infl.}$ 582, 634 mμ). The infrared spectra of 2 : 4-dimethyl-8-*iso*propylazulene and zierazulene, measured in chloroform solution, were identical. The proof that zierazulene has the structure (I) establishes it as the third known, fundamentally different, C_{15} natural azulene.

The visible spectrum of the above-mentioned methylzierazulene indicated that the new methyl group had entered the 6-position: reduction and dehydrogenation of the ester (IX; R = CO_2Et) should give 2 : 4 : 6-trimethyl-8-*iso*propylazulene, the proposed structure.

In every case so far reported, *e.g.*, 4 : 8-dimethyl-6-*iso*propylazulene [10] and 4 : 8-dimethylazulene-6-aldehyde,[11] diazoacetic ester has attacked the 5 : 6-positions of 4 : 7-disubstituted indanes (IV), and the resulting esters can be used to prepare 6-substituted azulenes. Reduction of the ester (IX; R = CO_2Et) with lithium aluminium hydride gave the hydroxymethyl compound (IX; R = CH_2·OH), which on dehydrogenation with palladium–charcoal gave a reddish-violet oil. Isolation in the usual way gave an azulene fraction whose *s*-trinitrobenzene adduct, m. p. 130—138°, appeared to be heterogeneous. Paper chromatography [12] (see p. 534) of the crude azulene gave two spots whose R_F values were identical with those of pure zierazulene and the methylzierazulene. The presence of zierazulene must be due to partial elimination of the hydroxymethyl group during dehydrogenation. Repeated crystallisation of the crude adduct from ethanol gave the 2 : 4 : 6-trimethyl-8-*iso*propylazulene–*s*-trinitrobenzene complex, whose m. p., 155—157°, was undepressed on admixture with the methylzierazulene adduct. Pure 2 : 4 : 6-trimethyl-8-*iso*propylazulene (II), obtained by chromatography on alumina of its pure *s*-trinitrobenzene adduct in *cyclo*hexane, gave a picrate whose m. p. and mixed m. p. with the methylzierazulene picrate was 138—140°. The visible spectrum of 2 : 4 : 6-trimethyl-8-*iso*propylazulene (II) in *cyclo*hexane ($\lambda_{max.}$ 536 mμ, $\lambda_{infl.}$ 570, 623 mμ) was identical with that of the methylzierazulene ($\lambda_{max.}$ 534 mμ, $\lambda_{infl.}$ 570, 622 mμ); and the infrared spectra of the two hydrocarbons measured in chloroform solution were identical. The relatively intense band at 859 cm.$^{-1}$ shown by 2 : 4 : 6-trimethyl-8-*iso*propylazulene is not shown by 2 : 4-dimethyl-8-*iso*propylazulene.

Experimental

Visible spectra were measured for *cyclo*hexane solutions by using a Hardy recording spectrophotometer. Infrared spectra were measured with a Perkin-Elmer double-beam spectrophotometer. Light petroleum refers to the fraction of b. p. 60—90°.

α-*Methyl*-β-(2-*methyl*-5 iso*propyl*)*propionic Acid* (V).—To powdered sodium (2·3 g.) in dry xylene (40 ml.) was slowly added ethyl methylmalonate [13] (17·4 g.), and the mixture refluxed for 2 hr. To the vigorously stirred mixture (at room temperature) was added 2-chloromethyl-*p*-cymene [7] (18·2 g.; b. p. 143—147°/50 mm.) during 15 min. After refluxing for a further 6 hr., the mixture was cooled and acidified with a small amount of acetic acid, and water (100 ml.) was added. The product was isolated with ether. Fractional distillation gave a small forerun and then the malonic ester (18·8 g., 59%), b. p. 149—160°/1 mm. Rapson and Short [9]

[10] Plattner and Roniger, *Helv. Chim. Acta*, 1943, **26**, 905.
[11] Arnold and Pahls, *Chem. Ber.*, 1954, **87**, 257.
[12] Knessl and Vlastiborová, *Coll. Czech. Chem. Comm.*, 1954, **19**, 782.
[13] "Organic Reactions," Coll. Vol. II, John Wiley and Sons, New York, 1955, p. 279.

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give b. p. 181—185°/8 mm. The ester was hydrolysed for 3 hr. with a solution from sodium (28 g.) in refluxing 95% ethanol (550 ml.). Water (600 ml.) was added and the bulk of the ethanol removed by distillation. Working up in the usual way gave a brown oil which crystallised. Recrystallisation of a small amount from aqueous methanol gave the malonic acid as needles, m. p. 173°. Rapson and Short [9] record m. p. 170°. The bulk of the crude dicarboxylic acid was heated at 180°; distillation then gave the acid (V) (61·4 g., 93%), b. p. 159—160°/2 mm. Rapson and Short [9] record b. p. 190—195°/14 mm.

The *amide*, plates from ethanol, had m. p. 107·5° (Found: C, 76·7; H, 9·6. $C_{14}H_{21}ON$ requires C, 76·7; H, 9·6%).

2 : 4-*Dimethyl*-7-iso*propylindan*-1-*one* (VI).—The acid (V) (70 g.) and thionyl chloride (70 g.) were heated at 80—90° for ½ hr. Excess of thionyl chloride was removed by raising the bath-temperature to 160°, and distillation gave the acid chloride (73 g., 96%), b. p. 109—111°/1 mm. This (78·5 g.) was added dropwise with stirring to finely ground anhydrous aluminium chloride (47 g.) in pure dry benzene (80 ml.) during 1¼ hr. at >35°. After being stirred for a further 4 hr., the mixture was poured on ice (400 g.), concentrated hydrochloric acid (100 ml.) added, and the mixture shaken. Isolation with ether and distillation gave 2 : 4-*dimethyl*-7-iso*propylindan*-1-*one* (VI) (62·4 g., 94%), b. p. 111—114°/1 mm., n_D^{15} 1·5429 (Whittleston [7] records b. p. 147—150°/9 mm., but the ketone was not analysed or characterised) (Found: C, 83·3; H, 9·0. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%). The 2 : 4-*dinitrophenylhydrazone*, m. p. 186°, was obtained as brilliant red hexagonal plates from ethanol (Found: C, 62·4; H, 5·6. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8%).

2 : 4-*Dimethyl*-7-iso*propylindan*-1-*ol* (cis *and* trans) (VII).—The foregoing indanone (2·0 g.) in dry ether (20 ml.) was added slowly to a suspension of lithium aluminium hydride (0·8 g.) in dry ether (60 ml.), and the mixture refluxed 1½ hr. Working up in the usual way gave a viscous oil, which was dissolved in light petroleum and adsorbed on alumina (30 g.). Elution with light petroleum (300 ml.) gave a viscous, colourless oil (620 mg.) which slowly crystallised. Recrystallisation from *n*-hexane gave 2 : 4-*dimethyl*-7-iso*propylindan*-1-*ol* (VII) as needles, m. p. 84·5° (Found: C, 82·3; H, 9·9. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%).

Elution of the column with ether–light petroleum (3 : 2) gave a further 70 mg. of viscous oil. Crystallisation from *n*-hexane gave the *isomer* as fleecy needles, m. p. 79·5° (Found: C, 82·3; H, 9·9%). A mixture of the *cis-trans*-isomers melted at 74°.

2 : 4-*Dimethyl*-7-iso*propylindane* (VIII).—To amalgamated zinc wool (150 g.), concentrated hydrochloric acid (150 ml.), and water (115 ml.) was added the indanone (VI) (58·4 g.), and the mixture was refluxed for 17 hr. (50 ml. portions of acid were added at 3 hr. intervals). The cooled mixture was decanted and the metal washed with ether. The ether washings, together with an ether extract of the aqueous suspension, were washed successively with water, 10% sodium hydroxide solution, and water, and dried (Na_2SO_4). After removal of the solvent, distillation from sodium gave 2 : 4-*dimethyl*-7-iso*propylindane* (VIII) (51·4 g., 95%), b. p. 94°/1·5 mm., n_D^{15} 1·5202 (Found: C, 89·7; H, 10·8. $C_{14}H_{20}$ requires C, 89·3; H, 10·7%).

2 : 4-*Dimethyl*-8-iso*propylazulene* (I).—The foregoing indane (15 g.) was heated at 135°, and diazoacetic ester (4 g.) added dropwise with shaking during 15 min. The temperature was then raised to 160° during 2 hr. and kept there for another hour. Evolution of nitrogen became vigorous at 140° and the mixture turned dark red above 145°.

Fractional distillation gave unchanged starting material (12·6 g.), b. p. 80—120°/1 mm., a dark red viscous oil (2·75 g.), b. p. 120—175°/1 mm., and a dark brown viscous residue (1·35 g.).

Recovered indane was recycled twice, giving a further 2·0 g. of the required ester (IX), b. p. 120—175°/1 mm., and a dark brown residue (4·5 g.). The total yield of the crude ester was 4·75 g. (23%). The dark brown residues from this and subsequent experiments were combined and distilled, giving more of the required ester.

The ester (9·4 g.) was refluxed in a solution from sodium (3·3 g.) in 95% ethanol (70 ml.) for 1 hr. Water (70 ml.) was added, refluxing continued for ½ hr., and the bulk of the alcohol removed. Isolation in the usual way gave 1 : 2 : 3 : 5(7)-tetrahydro-2 : 4-dimethyl-8-*iso*propylazulene-6-carboxylic acid as a brown viscous oil (4·6 g.).

The crude acid (4·6 g.) was heated under nitrogen with 10% palladium–charcoal (460 mg.) at 250° for 2 hr. Azulene formation began when the temperature had reached 230° and the mixture rapidly became deep violet. The cooled mixture was extracted with light petroleum and chromatographed on alumina. The violet eluate was purified by several successive extractions from light petroleum solution into cold syrupy phosphoric acid, which persistently

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became deep red. The deep violet oil (700 mg., 19·8%) thus obtained was treated with *s*-trinitrobenzene (720 mg.) in ethanol (30 ml.), giving an adduct (940 mg.), m. p. 119°. Two recrystallisations from ethanol gave a product of m. p. 120° which was dissolved in light petroleum and chromatographed on alumina. The violet eluate was extracted into phosphoric acid, which then became only pale yellow. The purified 2 : 4-dimethyl-8-*iso*propylazulene (I), recovered as before, was converted into its *s-trinitrobenzene adduct*, which crystallised from ethanol as fine maroon needles, m. p. 122·5°, undepressed on admixture with zierazulene–*s*-trinitrobenzene adduct (Found: C, 61·7; H, 5·2. $C_{21}H_{21}O_6N_3$ requires C, 61·3; H, 5·1%). The *picrate* crystallised as fine dark brown needles (from ethanol), m. p. 118°, undepressed on admixture with zierazulene picrate (Found: C, 58·9; H, 4·9. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%).

For the measurement of spectra, 2 : 4-dimethyl-8-*iso*propylazulene was recovered from the pure *s*-trinitrobenzene adduct by chromatography on alumina in spectroscopically pure *cyclo*hexane: (*a*) Visible (in *cyclo*hexane): $\lambda_{max.}$ 545 mμ, $\lambda_{infl.}$ 582, 632 mμ (zierazulene showed [1] $\lambda_{max.}$ 549 mμ, $\lambda_{infl.}$ 582, 634 mμ). (*b*) Infrared (in $CHCl_3$): $\nu_{max.}$ 1575s, 1510s, 1475m, 1458m, 1393w, 1384w, 1371w, 1321s, 1192w, 1125w, 1032m cm.$^{-1}$ (identical with the spectrum of zierazulene).

2 : 4 : 6-*Trimethyl*-8-iso*propylazulene*.—The ester (IX; R = CO_2Et) (5·0 g.) in dry ether (10 ml.) was added to lithium aluminium hydride (1·5 g.) in dry ether (100 ml.). The mixture was refluxed for ½ hr., and the complex decomposed in the usual manner. After being washed with water and dried (Na_2SO_4), the ether solution gave the crude hydroxymethyl compound as a brown viscous oil (3·5 g.)

The alcohol (3·5 g.) and 10% palladium–charcoal (350 mg.) were heated to 240°. After the initial vigorous reaction, the temperature was raised to 255° for 1½ hr., then to 290° for a further 15 min. The reddish-violet mixture was extracted with light petroleum and chromatographed on alumina, and the azulene fraction purified as before by several successive extractions into syrupy phosphoric acid. The azulene thus obtained (620 mg., 19·4%) was treated with *s*-trinitrobenzene (650 mg.) in ethanol (30 ml.), giving an adduct of m. p. 130—138°). Paper chromatography (see below) showed that it was a mixture, and that the contaminant was 2 : 4-dimethyl-8-*iso*propylazulene. After seven recrystallisations from ethanol the *s*-trinitrobenzene adduct of 2 : 4 : 6-*trimethyl*-8-iso*propylazulene* (II) was obtained as fine reddish-brown needles, m. p. and mixed m. p. with the methylzierazulene adduct, 155—157° (Found: C, 62·0; H, 5·3. $C_{22}H_{23}O_6N_3$ requires C, 62·1; H, 5·4%). The *picrate* was brown needles (from ethanol), m. p. and mixed m. p. 138—140° (Found: N, 9·5. $C_{22}H_{23}O_7N_3$ requires N, 9·5%). Spectroscopic samples were prepared in a similar manner to those of 2 : 4-dimethyl-8-*iso*propylazulene: (*a*) Visible (in *cyclo*hexane): $\lambda_{max.}$ 534 mμ, $\lambda_{infl.}$ 570, 622 mμ (methylzierazulene showed [1] $\lambda_{max.}$ 534 mμ, $\lambda_{infl.}$ 570, 622 mμ). (*b*) Infrared (in $CHCl_3$): $\nu_{max.}$ 1586s, 1510s, 1470m, 1458m, 1394m, 1384m, 1374w, 1334m, 1316w, 1204w, 1155w, 1087w, 1034w, 859m cm.$^{-1}$ (identical with the infrared spectrum of the methylzierazulene).

Paper Chromatography of Natural and Synthetic Zierazulenes.—The method used was that of Knessl *et al.*[12] Whatman No. 1 paper was impregnated with pure paraffin oil by soaking in a 20% (v/v) paraffin–light petroleum solution for a few min., then drying between filter papers. To determine the approximate paraffin content of the paper (which should be 1·8—2·4 mg./sq. cm.), a strip of paper of known area and weight was treated similarly and reweighed. The mobile phase was 55% (w/w) phosphoric acid. On paper with a paraffin content of 1·97 mg./sq. cm. and a development time of 48 hr., synthetic and natural zierazulene had R_F 0·33. Under the same conditions, the synthetic and the natural methylzierazulene had R_F 0·60.

I am indebted to Professor A. J. Birch, F.R.S., for helpful advice. Microanalyses were carried out by Miss B. Stevenson. For infrared and visible spectra I am indebted to Timbrol Ltd., and the National Standards Laboratory, C.S.I.R.O., Sydney, respectively.

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111. *Adsorption at Inorganic Surfaces. Part IV.* Mechanism of Adsorption of Organic Solutes by Chromatographic Alumina.*

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Organic solutes are adsorbed by chromatographic alumina mainly by hydrogen-bond formation, ion exchange, and chelation. In non-ionic compounds proton-donor groups (*e.g.*, –OH, $-NH_2$, and some activated $\geqslant CH$ groups) have the highest affinity, and proton-acceptor groups are adsorbed weakly, probably by bonding with the small content of aluminium hydroxide in the substrate. Sulphonated azo-dyes are readily adsorbed by acid-treated alumina; the reaction has a very small temperature coefficient and is probably mainly ion-exchange. Trisulphonate ions may be orientated flat as a monodisperse layer, but mono- and di-sulphonates appear to be adsorbed partly as anionic micelles. Adsorption is complete in less than 5 min. in the cold; the kinetics are consistent with the rate-controlling factor's being exchange of dye anions for inorganic anions across a thin liquid boundary film around the alumina particles. There is no evidence of any adsorption in internal pores. Solvents, *e.g.*, ethanol or water, with hydrogen-bond affinity for solute or substrate, or those with van der Waals attraction for the solute, reduce affinity by competition.

This paper describes an investigation into the mechanism by which chromatographic alumina adsorbs organic non-ionic and ionic solutes. The substrate, prepared by low-temperature (<700°) dehydration of alumina trihydrate, is a mixture of γ-alumina and a little alumina monohydrate (Al_2O_3,H_2O) with some sodium carbonate. High-temperature ignition (>900°) completes the dehydration and produces the less active α-alumina.[1] The adsorbing power of the technical material is often classified by the rate of travel of azobenzene and certain of its simple derivatives in non-aqueous solution down a column under standardised conditions.[2,3] Grade I represents highest and Grade III lowest activity (*i.e.*, most rapid passage of solute); Grade III can be prepared from Grades I and II by adding a little water.

When water is the solvent the reaction of the alumina—whether acid or alkaline—considerably affects its adsorptive powers; bases are adsorbed better on alkaline than on acid alumina and acids show the opposite behaviour.[3,4]

Relation between Structure and Adsorption Effects.—(i) *Non-ionic solutes.* Much information is available upon the relative order in which organic solutes separate on the alumina column.[1,5] Strong adsorption (slow passage) is favoured generally by high polarity, by an increase in the number of polar substituents or of aromatic nuclei, and by the absence of internal chelation (*i.e.*, with such groups as amino-, hydroxy-, or thiol in anthraquinone or azo-compounds).[3,6,7,8] Configuration also influences adsorption (*cis*- but not *trans*-azobenzene is adsorbed from light petroleum [9]). A solute may undergo catalytic change (*e.g.*, deacetylation) on an alumina column, or it may isomerise. Thus, several compounds which are colourless in cold benzene become highly coloured when adsorbed on alumina

* Part III, *J. Appl. Chem.*, 1958, **8**, 416.

[1] Cassidy, "Fundamentals of Chromatography. Technique of Organic Chemistry, Vol. X," Interscience Publishers, Inc., New York, N.Y., 1957.
[2] Brockmann and Schodder, *Ber.*, 1941, **74**, *B*, 73.
[3] Brockmann, *Discuss. Faraday Soc.*, 1949, **7**, 58.
[4] Hesse and Sauter, *Naturwiss.*, 1947, **34**, 250, 251, 277.
[5] *E.g.*, Strain, "Chromatographic Adsorption Analysis," Interscience Publishers Inc., New York, N.Y., 1942.
[6] Hoyer, *Kolloid-Z.*, 1951, **121**, 121.
[7] Rao, Shah, and Venkataraman, *Proc. Indian Acad. Sci.*, 1951, **34**, *A*, 355.
[8] Williams, "An Introduction to Chromatography," Blackie and Son Ltd., London, 1946.
[9] Hillson and Birnbaum, *Trans. Faraday Soc.*, 1952, **48**, 478.

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(*e.g.*, 1 : 3-dioxoindanes enolise, and *spiro*pyrans become heteropolar, in both cases with development of colour [10]).

Basu [11] recently suggested that adsorption of organic compounds on alumina is a form of molecular complex formation, and that the process is facilitated by (*a*) a high electron affinity of one component and (*b*) a low ionisation potential of the other. On the assumption that the energy of the top filled orbital of a conjugated organic molecule calculated by the LCAO method gives a rough estimate of (*b*), the position on the column of two series of compounds, *viz.*, five condensed-ring aromatic hydrocarbons and four αω-diphenylpolyenes, in both cases agrees with this hypothesis.

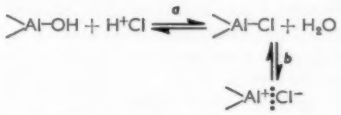
(ii) *Ionic solutes.* Investigations on adsorption of ionic solutes have been concerned mainly with dyes. Several authors [12–17] have studied qualitatively the effect of substitution in anionic dye molecules upon their ease of adsorption from water by alumina or aluminium hydroxide. Roosens,[18] who comprehensively surveyed previous work, defined the following general rules for adsorption of sulphonated azo-dyes: the greater the number of azo-groups, the stronger the adsorption; an amino- or a hydroxy-group is more effective when in the 2-position in the naphthalene nucleus (as second component) than in the 1-position; *o*-hydroxyazo-dyes are adsorbed more strongly than *p*-hydroxyazo-dyes; dyes containing a thio- or a hydroxyl group are more strongly absorbed than dyes free from those groups; the longer the wavelength at which the compounds adsorb light, the higher is the adsorption zone, in general, in the column; the greater the molecular weight, the stronger the adsorption; halogen substituents promote adsorption; and the more double bonds in the molecule, the stronger the adsorption. Also, the strength of adsorpton in the column increases with the number of sulphonate or of vinyl groups in the dye; [13] adsorption is weakened by a sulphonate group in the 8-position in phenylazo-2-naphthol dyes or *ortho*- to the central carbon atom in naphthyldiphenylmethane dyes; [15] the presence of phosphate ion in solution reduces adsorption of a sulphonated dye on hydrated alumina; [17] and there is some parallelism between adsorption and substantivity for cotton or rate of diffusion through gelatin.[13] Amongst sulphonated intermediates, 3-hydroxynaphthalene-1-sulphonic acid is adsorbed more strongly than 4-hydroxynaphthalene-1-sulphonic acid.[13]

Adsorption of inorganic ions. Several suggestions have been made to account for adsorption of inorganic ions by technical alumina. Chromatographic alumina normally is alkaline and contains sodium ions which exchange with cations in solution,[19] though even pure alumina adsorbs cations to some extent,[20] probably initially by an aluminium–hydrogen ion exchange.[21] Alumina can, in fact, function as an amphoteric ion-exchanger, *e.g.*, with cuprous chloride, but its normal sodium ion content makes it more effective in cation exchange.[22] Adsorption affinity rises with polarisability of the adsorbed ion or of groups co-ordinated with it.[21,23]

Anions are readily adsorbed on alumina pre-treated with hydrochloric acid. Wieland [24] explains this as an anion-exchange with the chloride ions taken up from the acid.

[10] Schönberg and Asker, *Science*, 1951, **113**, 56; Schönberg, Mustafa, and Asker, *J. Amer. Chem. Soc.*, 1951, **73**, 2876; 1952, **74**, 5640; 1953, **75**, 4645.
[11] Basu, *Chem. and Ind.*, 1956, 764.
[12] Mutch, *Quart. J. Pharm. Pharmacol.*, 1946, **19**, 490.
[13] Ruggli and Jensen, *Helv. Chim. Acta*, 1935, **18**, 624; 1936, **19**, 64.
[14] Ruiz, *Ind. parfum.*, 1946, **1**, 187; *Chem. Abs.*, 1948, **42**, 5675.
[15] Ruiz, Chovin, and Moureau, *Bull. Soc. chim. France*, 1946, **13**, 592.
[16] Weiser and Porter, *J. Phys. Chem.*, 1927, **31**, 1704.
[17] White and Gordon, *ibid.*, 1928, **32**, 380.
[18] Roosens, *Ind. Chim. Belg.*, 1952, **17**, 211, 339.
[19] Schwab and Jockers, *Naturwiss.*, 1937, **25**, 44.
[20] Fricke and Neugebauer, *ibid.*, 1950, **37**, 427.
[21] Sacconi, *Discuss. Faraday Soc.*, 1949, **7**, 173.
[22] Jacobs and Tompkins, *Trans. Faraday Soc.*, 1945, **41**, 388, 395, 400.
[23] Venturello and Agliardi, *Chimica e Industria*, 1944, **26**, 72.
[24] Wieland, *Z. physiol. Chem.*, 1942, **273**, 24.

Source of zeta-potential. O'Connor, Johansen, and Buchanan [25] studied the electrokinetic properties of corundum (natural alumina) before and after various mechanical and heat treatments and treatments with solutions of acids, alkalis, and salts. Normally the zeta-potential in water is positive, which these authors attribute to the presence of a layer of $Al(OH)_3$ formed from chemically bound water, and resistant to very high temperatures: this releases hydroxyl ions into the diffuse layer and the oxide then has a surface of positively charged aluminium atoms. Pre-ignition at above 1000° gives a material (α-Al_2O_3) with negative zeta-potential in water, probably owing to a layer of the weakly acidic AlO·OH. Treatment with hydrochloric acid appeared to produce a surface consisting of covalently bound and ionised chloride:



Reaction (*b*) (formation of ionised chloride) is favoured by increase in acid concentration.

Experimental

Preparation of Substrate.—The substrate was mainly from a single sample of chromatographic alumina (Type H, Savory and Moore), but a few tests were made on another, coarser, sample. In its original state the former was alkaline (20 c.c. of distilled water shaken with 1 g. of powder at room temperature had pH 9·5). It adsorbed cationic dyes but not anionic ones, unless previously acidified. Consequently all the material used was before use washed twice with hydrochloric acid (100 g. in 200 c.c. of 2N-acid) and then rinsed several times with water. It was then over-dried at 150° for several days, and stored in a desiccator ($CaCl_2$); 20 c.c. of distilled water shaken with 1 g. of treated powder at room temperature had pH 4·4; activity: Grade II.

	Type H	Coarse powder
Loss on ignition	6·5	5·9
Sieve grading (%) +100	0·6	8·8
−100, +150	67·0	57·7
−150, +200	18·1	25·5
−200	14·3	8·0
pH of 5% w/v solution	8·7	9·2
Activity	I—II	II
Temp. of activation:		
normal	600°	—
max.	700°	—
Specific surface area, cm.^{2} g.$^{-1}$ (approx.) (phenol adsorption calc. from Fig. 1)	$5{\cdot}0 \times 10^5$	$0{\cdot}5 \times 10^5$
(air-permeability test)	$0{\cdot}027 \times 10^5$	$0{\cdot}004 \times 10^5$
(microscopical counts)	$0{\cdot}035 \times 10^5$	$0{\cdot}15 \times 10^5$

Characteristics of the substrates are tabulated. Air-permeability tests and microscopical counts gave specific surface areas less by factors of *ca.* 100 and 10, respectively, than those given by phenol adsorption. The discrepancies between the various area values could be explained by assuming (*a*) that the H-type powder has a much rougher surface than the other, and perhaps a higher content of extremely fine particles (note the fine sieve gradings), (*b*) that in the air-permeability test fine particles tend to lodge in cracks in the rough surface of coarse ones (especially of type H), and (*c*) that loss on ignition represents water molecules located inside the crystal rather than those adsorbed at the outer surface.

The solutes and solvents were purified normally, and water was distilled; benzene and 2 : 2 : 4-trimethylpentane were dried over sodium. The azo-dyes were mainly obtained from commercial sources, except (VI), (VII), and (X), which were laboratory preparations. The 1-acetamido-8-hydroxynaphthalene-3 : 6-disulphonic acid for (VI) and (VII) was prepared as described by Fierz-David and Blangey.[26] The dyes were purified to >95% ($TiCl_3$ analysis) by

[25] O'Connor, Johansen, and Buchanan, *Trans. Faraday Soc.*, 1956, **52**, 229.
[26] Fierz-David and Blangey, "Fundamental Processes of Dye Chemistry," Interscience Publishers Inc., New York, N.Y., 1949.

salting-out from aqueous solution with sodium chloride, followed by recrystallisation from aqueous ethanol.

Adsorption Procedure.—0·1 g. samples of alumina and 5 c.c. of test solution in sealed glass tubes were tumbled at 35 r.p.m. in a thermostat.[27] Equilibrium is attained rapidly. The solutions were analysed after 10—15 minutes' agitation, the tubes being first left to stand vertically in the thermostat until the powder settled, and the solution then decanted through filter paper. Amounts of solute adsorbed were calculated from analyses of solutions before and after treatment.

In rate measurements it was possible to obtain reproducible results for times down to 10 sec. by using mechanical agitation, if the solution had previously reached temperature equilibrium in the thermostat. Variation in volume of the aqueous dye solutions from 2·5 to 20 c.c. did not affect the isotherms. No dissolved alumina was detected (by Aluminon) after shaking 0·1 g. of powder (H) with 5 c.c. of distilled water for up to 24 hr. at 18°. (The isotherms for adsorption on *anodic* alumina vary considerably with the liquid : solid ratio used, attributed to etching by the solution, the film oxide being very slightly soluble in water.[28])

Analysis.—Cellobiose and sucrose were determined by refractometry on a Pulfrich (Bellinghan and Stanley) instrument, in sodium light. All other solutes were determined absorptiometrically on a Hilger Spekker or a Unicam S.P. 500 or S.P. 600 instrument. The lowest measurable adsorption is *ca.* 0·01 mmole/kg. of Al_2O_3.

Results and Discussion

Results are summarised in Tables 1 and 2 and Figs. 1—5.

Evidence for Hydrogen-bond Adsorption of Non-ionic Solutes.—Evidence from this and earlier work that hydrogen-bonding is the principal force responsible for adsorption of non-ionic solutes can be summarised thus: (*a*) The anodic film on aluminium adsorbs non-

Table 1. *Behaviour of non-ionic solutes towards chromatographic alumina.*

Solute	Solvent *	Reaction †	Solute	Solvent *	Reaction †
trans-Azobenzene	B, AE	N	Phenylazo-2-naphthylamine	D	A
cis-Azobenzene	AE, P	A[9]	2 : 4-Diacetoxyazobenzene	B	A
Bis(phenylazo)benzene	B, AE,	N	Phenol	W	A
(*trans*?)	BE, BB		Resorcinol	W	A
,, ,,	O	A	Sucrose	W	N
Bis(phenylazo)benzene (*cis*?)	AE	A	*m*-Nitroaniline	AE′	A
Cellobiose	W	A	*p*-Nitroaniline	AE′	A
Chlorobenzene	B	N	Nitrobenzene	AE′	S
4-Aminoazobenzene	D	A	,,	B	N
2 : 4-Dihydroxyazobenzene	E	A	Terephthalaldehyde	B	A

Conditions: Solutions *ca.* 0·001—0·01M; temp. 20—60°; time, 5—30 min.

* B, Benzene; AE, ethanol–water (4 : 1 v/v); AE′, ethanol–water (1 : 1 v/v); BE. benzene-ethane-1 : 2-diol; BB, benzene–butane-1 : 4-diol; O, 2 : 2 : 4-trimethylpentane; D, dioxan; E, ethanol; P, light petroleum; W, water.

† A, adsorbed; N, not adsorbed; S, slightly adsorbed.

ionic solutes mainly by hydrogen bonds.[29] This film is chemically very similar to the present substrate. (*b*) The adsorption of simple non-ionic anthraquinones and azo-compounds on alumina columns (judged by speed of travel) is weaker when any amino-, hydroxy-, etc., groups they contain are internally chelated, than when they are free.[6] (*c*) The behaviour towards non-ionic compounds of the alumina powder here used is very similar to that of the anodic film, *i.e.*, proton donors are readily adsorbed and proton acceptors adsorbed weakly or not at all. (It is assumed that acetyl and aldehyde groups act as proton donors.[30]) (*d*) The evidence of isotherm shapes agrees with that given by

[27] (*a*) Allingham, Cullen, Giles, Jain, and Woods, *J. Appl. Chem.*, 1958, **8**, 108; in this paper, the analysis of the MSC fine silica powder used should be: SiO_2, 96·5; Al_2O_3, 2·5; Fe_2O_3, CaO, MgO, alkali, etc. 1%. Also in Table I, first footnote, and Figs. 2, 6, and 7, *y*-axes, units should read mmole/kg.; (*b*) Galbraith, Giles, Halliday, Hassan, McAllister, Macaulay, and Macmillan, *ibid.*, 1958, **8**, 416.

[28] Stewart, Ph.D. thesis, Glasgow, 1957, 481.

[29] Giles, Mehta, Stewart, and Subramanian, *J.*, 1954, 4360.

[30] Arshid, Giles, and Jain, *J.*, 1956, 559, 1272.

TABLE 2. *Adsorption of sulphonated azo-dyes on chromatographic alumina.*

Dye	Max. ads. (mmole/kg.)	Found Dev. (%) (*a*) †	Cross-sectional area of anion (Å²) * Calc. End-on	Edge-on	Flat	Found Dev. (%) (*b*) †	$-\Delta\mu$ (kcal./mole)	$-\Delta S$ (cal./mole/deg.) (50°)	$-\Delta E_A$ (kcal./mole)
				Monosulphonates					
(I)	166	−13	*50*	80	150	−57	8·3 ± 0·5	25·5 ± 1·5	—
(II)	175	−8	*50*	75	150	−48	12·3 ± 0·5	38 ± 1·5	9·2
				Disulphonates					
(III)	104	−18	65	*80*	190	−57	21·0 ± 1·5	65 ± 4·5	13·0
(IV)	100	−20	60	*80*	190	−63	20·0 ± 0·5	62 ± 1·5	12·5
(V)	80	−36	60	*85*	195	−92 (+18, flat)	19·0 ± 0·5	58·5 ± 1·5	—
(VI)	132	+6	60	*85*	220	−15	17·0 ± 0·2	52·5 ± 0·5	—
(VII)	124	0	60	*85*	250	−24	18·0 ± 0·2	56 ± 0·5	—
(VIII)	106	−15	*65*	140	375	−89	19·3 ± 0·2	60 ± 0·5	3·2
(IX)	62	−50	55	*110*	235	−92	19·8 ± 0·2	61 ± 0·5	3·9
				Trisulphonates					
(X)	58	−8	65	85	*225*	0	31·0 ± 1·5	96 ± 4·5	1·4
(XI)	68	+8	55	80	*190*	0	26·5 ± 0·5	82 ± 1·5	—

* Area of smallest enclosing rectangle, measured by Catalin (Stuart-type) molecular models (no allowance for interlocking); most probable (monodisperse) orientation in italics.

† Deviation from theoretical values (*a*) for micellar adsorption, a mean value of 63 mmole/kg. being assumed for trisulphonates, equivalent to 125 and 190 mmole/kg. for di- and mono-sulphonates; (*b*) for orientated monodisperse adsorption (total surface coverage), values for trisulphonate dye X being assumed to represent a complete monolayer.

The amounts of *monodisperse* adsorbed anions should be inversely proportional to their appropriate cross-sectional areas, but the amounts of *micellar* adsorbed anions should be inversely proportional to their basicity, on the assumption that each sulphonate group is exchanged with one chloride ion, of which there is a limited supply.

other hydrogen-bond adsorptions.[31] Thus where there are two polar groups of similar affinity [*e.g.*, bis(phenylazo)benzene, resorcinol, terephthalaldehyde] the isotherm has the normal (L) shape, but where one group has much stronger hydrogen-bond affinity than any other in the molecule (*e.g.*, *cis*-azobenzene, cellobiose, phenol, nitroaniline) the curve is S-shaped. This appears to confirm that the main source of affinity is in the polar groups.

Hydrogen-bonding through $\geqslant$CH *Groups.*—The adsorption of cellobiose, 2 : 4-diacetoxyazobenzene, and terephthalaldehyde is attributed to $\geqslant$CH · · · bonding. Aldehyde and ester groups in solutes in aqueous or non-aqueous solutions can act as proton donors towards oxygen atoms in other solutes.[30] Some confirmation that this is the nature of the adsorption here is given by the difference in behaviour of cellobiose and sucrose. In water, cellobiose behaves monofunctionally as the open-chain aldehyde, and sucrose is unreactive towards other hydrogen-bonding solutes, because the hydroxy- and oxo-groups are protected by the solvent.[30] Similar behaviour is observed here in their reactions towards alumina, *i.e.*, cellobiose appears to be adsorbed as a monofunctional compound, giving as it does an S-shaped isotherm, and sucrose is not adsorbed.

There is of course the possibility that catalytic decomposition of these solutes in contact with alumina may occur, giving strongly adsorbed hydroxylic compounds; no evidence of decomposition could be obtained however by spectroscopy of solutions of 2 : 4-diacetoxyazobenzene before and after treatment with alumina, adsorption tests with cellobiose with acid and alkaline alumina (both appeared similarly effective), or pH measurement on distilled water shaken in air with a solution of terephthalaldehyde in benzene; there was no reduction in pH. No acid is therefore formed by air oxidation in *absence* of alumina. (Detection of oxidation on the column itself was not attempted.)

Proton-accepting Groups and Solvent Effects.—The hydroxide content of the powder is no doubt responsible for its slightly higher affinity for amino-, azo-, and nitro-groups than

[31] Cf. Giles and MacEwan, Second Internat. Cong. Surface Activity, London, 1957, **3**, 457.

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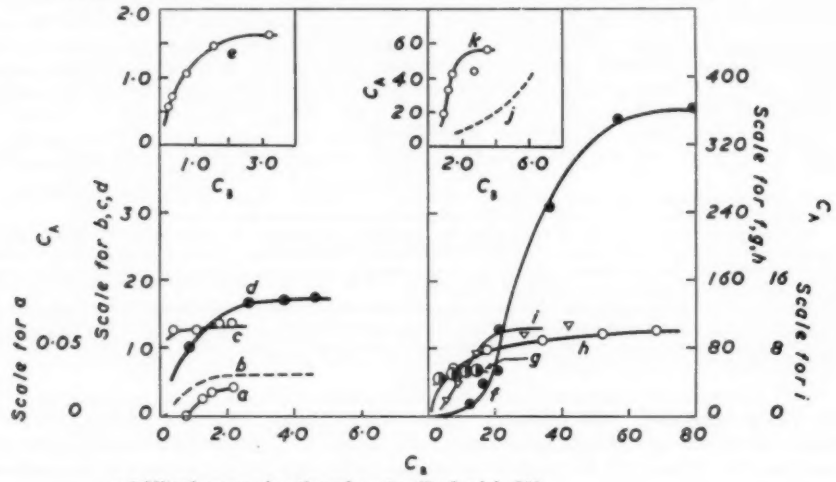
the anodic film (cf. Part I [29]). Even so, the affinity of these groups is low and subject to competition by the solvent; *e.g.*, *trans*-bis(phenylazo)benzene is adsorbed from 2 : 2 : 4-trimethylpentane, but not from benzene, where association will occur between the aromatic nuclei of solute and solvent, or from ethanol with which hydrogen-bonding can occur.

The greater ease of adsorption of *cis*- than *trans*-azobenzene * must be a steric effect, due to the more ready approach to the alumina surface of the *cis*-azo-group.

Sulphonated Azo-dyes.—The dyes were all sodium salts: (I) sulphanilic acid→2-naphthol (Orange II, C.I. 15510), (II) 4-aminonaphthalene-1-sulphonic acid→2-naphthol (C.I.15620),

FIG. 1. *Adsorption isotherms of non-ionic solutes on chromatographic alumina.*



a,* Nitrobenzene in ethanol–water (1 : 1 v/v), 20°.
b, *cis*-Bis(phenylazo)benzene in ethanol–water (4 : 1 v/v), 30°.
c, 2 : 4-Diacetoxyazobenzene in benzene, 44°.
d, 4-Aminoazobenzene in dioxan, 58°.
e,* Terephthalaldehyde in benzene, 20°.
f, Phenol in water, 58°.
g, Phenylazo-2-naphthylamine in dioxan, 58°.
h, Resorcinol in water, 58°.
i,* 4-Nitroaniline in ethanol–water (1 : 1 v/v), 20°.
j, *cis*-Azobenzene in ethanol–water (4 : 1 v/v), 30°.
k, Cellobiose in water, 53°.

C_A is the equilibrium concentration on the alumina (mmole/kg.) and C_B that in the bath (mmole/l.).
* Coarser alumina; all others chromatographic alumina.

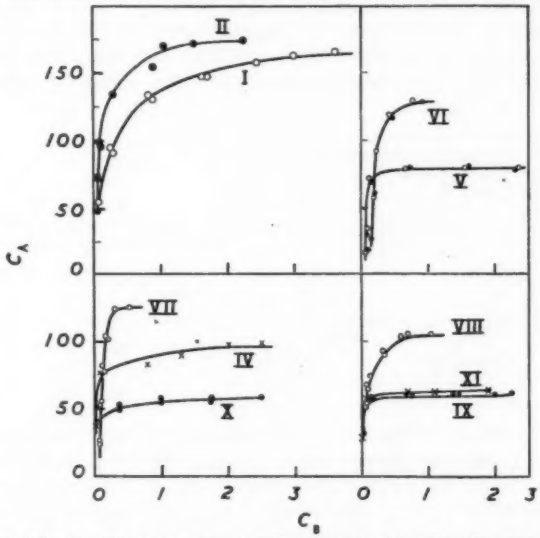
(III) 1-naphthylamine→2-hydroxynaphthalene-3 : 6-disulphonic acid (C.I. 16180), (IV) 4-aminonaphthalene-1-sulphonic acid→6-hydroxynaphthalene-2-sulphonic acid (C.I. 16045), (V) aniline→1-acetamido-8-hydroxynaphthalene-3 : 6-disulphonic acid (C.I. 18050), (VI) *p*-*n*-butylaniline→1-acetamido-8-hydroxynaphthalene-3 : 6-disulphonic acid, (VII) *p*-*n*-dodecylaniline→1-acetamido-8-hydroxynaphthalene-3 : 6-disulphonic acid, (VIII) phenol←*O*-ethyl ether of *o*-tolidine→2-aminonaphthalene-3 : 6-disulphonic acid (C.I. 23605), (IX) 4-(4-amino-*m*-tolylazo)toluene-3-sulphonic and→crocein acid (C.I. 27165), (X) sulphanilic acid→2-hydroxynaphthalene-3 : 6-disulphonic acid, (XI) 4-aminonaphthalene-1-sulphonic acid→7-hydroxynaphthalene-1 : 3-disulphonic acid (C.I. 16255).

* The isotherms for the two azobenzenes are shown without experimental points (Fig. 1). The solutions were exposed to light, to effect isomerisation to *cis*-forms, before adsorption, but some *trans*-isomers may have remained unchanged. The *x*-axis scale therefore refers to the combined total of both isomers.

Adsorption is very rapid, and the isotherms have well-defined plateaux with apparently no subsequent rise (Fig. 2). This suggests that a monolayer is formed on the outer surface of the alumina particles, with no penetration of the internal structure. The isotherms for different temperatures are identical, *i.e.*, the apparent heats of adsorption are all very low (<*ca.* 0·25 kcal./mole) (Fig. 2), consistent with ion-exchange adsorption. The shapes of the isotherms indicate that the anions have much higher affinity for the substrate than has the solvent (water).[31] *

Orientation of Adsorbed Dye Anions.—As stated, the shapes of the isotherms indicate that the adsorbed dye anions form a monolayer, and this could be composed either of

FIG. 2. *Adsorption isotherms of sulphonated azo-dyes from water on chromatographic alumina.*



Temperatures: I, 33°, 60°; II, 33°; IV, 26°; V, 50°, 60°; VI, 51°, 61°; VII, 50°, 60°; VIII, 49°, 61°; IX, 49°, 61°; X, 49°, 60°; IX, 26°. For clarity the points for individual temperatures are not differentiated in several cases. Roman numerals refer to dyes.

mono-disperse anions, each oriented with all sulphonate groups as close as possible to the surface, or of anionic micelles (cf. the cationic micellar adsorption of basic dyes by silica [27b]). On first principles it can be postulated that dyes capable of packing with large areas of aromatic nuclei in close association, *i.e.*, the mono- and some di-sulphonates, will form some micelles, whereas trisulphonates will orientate as single anions flat on the surface. The data (Table 2) are however not adequate to prove this hypothesis, though they appear to be in reasonable agreement with it; they indicate also that the acetamido-group in dye (V) may assist a flat orientation by hydrogen-bonding. (This is the only unalkylated dye used here containing a proton-donating group.) It seems probable from the quantitative data that all ionic compounds form some monodisperse orientated monolayer, but with decreasing charge on the molecule relative to its molecular weight there is an increasing tendency for the adsorbed layer to contain micelles. Differences in the amounts of the dyes adsorbed may be accounted for by differences in their anions' ability to pack in the monolayer.

* The initial portion of the isotherm for the dye with the long paraffin chain (VII) differs from that of its homologue (V) in being slightly convex to the *x*-axis (the scale of Fig. 2 is too small to show this); a similar difference between (V) and (VII) is observed on wool, on which adsorption is also by ion-exchange.

Dye Affinities.—The dyes (Na_zD) can be placed in an order of adsorption affinity and entropy by applying the expression $-\Delta\mu^\circ = -RT \ln [Na]_s^z[D]_s$, where $[Na]_s^z[D]_s$ is the dye activity in a solution at equilibrium with alumina containing dye at half its maximum adsorption. This expression is derived from the affinity equation for ion-exchange adsorption of acids and dyes by protein fibres (cf., *e.g.*, ref. 32) though it is not certain that if adsorption is micellar the values so obtained (Table 2) are true thermodynamic free energies.

The data show that additive " partial affinity " values can be assigned to sulphonate groups according to their orientation, *e.g.*, 12·0 ± 2·5, 6·8 ± 0·7, and 6·5 ± 1·0 for positions 3, 6, and 8 in the coupling component, and 12 ± 0·5 for position 4 or 4″ in the first component [except dye (I)]. The rise in apparent entropy with increased sulphonation must be attributed to increased configurational entropy.[33]

Rate Measurements.—Rate curves determined for several dyes over a range of temperature (Fig. 3) show that, as expected the adsorption rate rises with temperature. The kinetics of ion-exchange adsorption by small particles, assumed spherical, have been

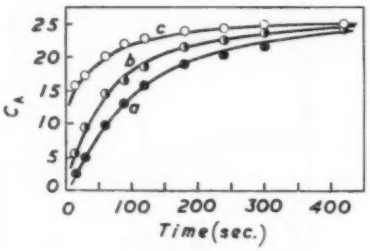


FIG. 3. *Rate curves for adsorption of dye* (II) *(0·2 g./l.) on chromatographic alumina.*

a, 9°; *b*, 14°; *c*, 25°.

studied by Boyd *et al.*[34] and Kressman and Kitchener,[35] using the Nernst static diffusion theory. A similar treatment is used here, it being assumed that adsorption involves transport of an ion from the bulk of the solution up to the boundary of a liquid film surrounding each particle, where anion exchange occurs at constant ionic concentration.

If the rate of adsorption is controlled by diffusion through the liquid boundary layer, the plot of log $[(1 - Q_t)/Q_\infty]$ against t should be linear, with a gradient proportional to the diffusion coefficient in this layer. (Q_t and Q_∞ are the quantities of anions exchanged after time t and at equilibrium.) Plots of this type for five dyes (Fig. 4) are linear over nearly the whole range of time and temperature. There are exceptions where the early stages of adsorption (20—60 sec.) give points deviating from linearity in a direction corresponding with values of Q_t lower than required by theory, *i.e.*, the initial rate of diffusion of chloride ion outward, and dye anion inward, is too low.

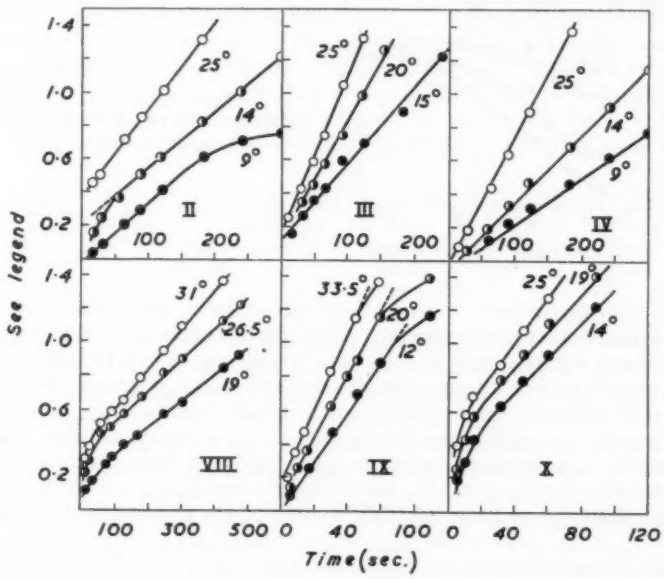
The very high rate of attainment of equilibrium adsorption on the powder indicates fairly clearly that no diffusion into internal pores occurs. In confirmation, rate measurements were tested by an expression developed for internal diffusion in an adsorbent particle[34,36-38] whereby a plot of Q_t/Q_∞ against $t^{\frac{1}{2}}$ should be linear. Kressman and Kitchener[35] find that this rule holds up to $Q_t/Q_\infty = 0{\cdot}8$ in some cases, but in general it can only be expected to hold for lower values. A plot of Q_t/Q_∞ against $t^{\frac{1}{2}}$ for one dye is given

[33] (*a*) Gilbert and Rideal, *Proc. Roy. Soc.*, 1944, *A*, **182**, 335; (*b*) Vickerstaff, " The Physical Chemistry of Dyeing," Oliver and Boyd Ltd., London and Edinburgh, 2nd edn., 1954.
[34] Everett, *Proc.*, 1957, 38.
[34] Boyd, Schubert, and Adamson, *J. Amer. Chem. Soc.*, 1947, **69**, 2818; Boyd, Adamson, and Myers, *ibid.*, p. 2836.
[35] Kressman and Kitchener, *Discuss. Faraday Soc.*, 1949, **7**, 90.
[36] Carslaw and Jaeger, " Conduction of Heat in Solids," Oxford Univ. Press, London, 1947.
[37] Paterson, *Proc. Phys. Soc.*, 1947, **59**, 50.
[38] Barrer, *Trans. Faraday Soc.*, 1949, **45**, 358.

in Fig. 5 and this plot shows that the agreement with theory for internal diffusion is less satisfactory than for the boundary-layer diffusion for the same dye (Fig. 4).

Activation Energy.—Plots of the values of the diffusion coefficient (calculated from the gradients of plots in Fig. 4) against the reciprocal of the absolute temperature are linear, and from the slopes of these lines the activation energies in the last column of Table 2 were calculated. The data are insufficient for any certain generalisation to be made, and clearly the relation between structure and activation energy is complex, but it

FIG. 4.—*Rate of adsorption of azo-dyes by chromatographic alumina plotted on liquid boundary film hypothesis.*



Vertical axis: $\log [(1 - Q_t)/Q_\infty]$.

appears that dyes with aromatic residues of similar shape, and the same number of ionic groups, tend to have similar activation energies.

Cationic Compounds.—The alkaline oxide adsorbs basic dyes. No quantitative work was carried out on this type of adsorption, but there appears no reason to doubt that the mechanism is one of cation exchange. Basic dyes will probably be adsorbed as cationic micelles, as they are by silica powder.[27a]

Chelating Dyes.—These are adsorbed with production of the colour of the aluminium chelate (scarlet with alizarin or sulphonated alizarin) so that, as in the case of the anodic film, adsorption must take place by direct formation of lakes with aluminium atoms in the alumina crystal lattice.

Conclusions.—Adsorption mechanism of non-polar solutes. Polynuclear aromatic hydrocarbons generally separate on the alumina column according to the number of their aromatic nuclei;[5,8] those containing the most nuclei are the less readily eluted. Two reasons can be suggested for this: (*a*) that a polar complex is formed between the alumina and the π-electrons of the hydrocarbon; (this resembles the mechanism suggested by Basu [11]), and (*b*) the rate of travel of the solute down the column is determined by the

rate of transfer of solute to the eluting solvent from the initial solvent holding the solute at the top of the column (a partition-chromatography effect).

Adsorption mechanism of polar and ionic solutes. The adsorption of most organic solutes, from water or non-aqueous solution, can be accounted for by the general principles revealed here. The main source of affinity of a non-ionic solute for alumina appears to be hydrogen-bonding through proton-donor groups in the solute. Proton-acceptor groups have low affinity, and probably form hydrogen-bonds with the hydroxide content of the substrate. Aldehyde and ester groups may act as proton-donors. The recorded observations (p. 535) on the relative order of separation of solutes on alumina columns can be

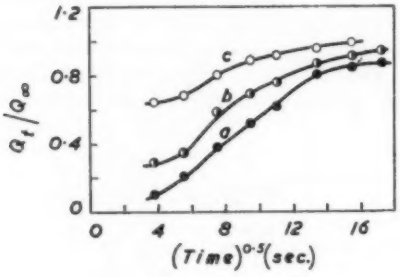


FIG. 5.—*Rate of adsorption of dye* (II) *plotted according to the pore penetration hypothesis.*
a, 9°; *b*, 14°; *c*, 25°.

explained on these hypotheses. Steric effects may occur in certain cases (*cis*-azobenzene is better adsorbed than the *trans*-isomer). The influence of the solvent is very important. Thus proton-donor solvents, such as ethanol or water, may reduce the affinity of a solute for alumina by being adsorbed preferentially themselves and so favour elution. Solvents which associate with the solute, either by hydrogen-bonding (*e.g.*, ethanol or water with polar solutes), or by van der Waals forces (*e.g.*, aromatic solvents with aromatic solutes), compete with the alumina for the solute and so favour elution. Proton-donor solvents will also compete with the solute for the substrate, *i.e.*, they will tend to deactivate the substrate by being adsorbed on sites on the alumina to the exclusion of the solute.

The reported more effective adsorption of *o*-aminoazo- or *o*-hydroxyazo-compounds than of their *para*-isomers is probably due to chelation with aluminium of the first-mentioned classes.

Adsorption mechanism of anionic solutes. The reaction of hydrochloric acid-treated oxide with anions is probably mainly exchange of chloride ions for the adsorbed anions, but some covalent bonding may also occur. Alumina which has been given other pre-treatments (*e.g.*, anodic film [29]) may have a greater tendency to adsorb anions by covalent bonding. This will be discussed elsewhere.

The authors thank Professor P. D. Ritchie for encouragement and interest; Dr. M. A. T. Rogers and Imperial Chemical Industries Limited, Dyestuffs Division, for gifts of intermediates and dyes; and Mr. M. H. Burn and Pharmaceutical Products Ltd., and Peter Spence and Sons Ltd., for analytical data on alumina.

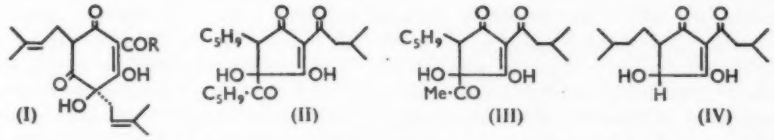
DEPARTMENT OF CHEMICAL TECHNOLOGY,
ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY, GLASGOW, C.1. [*Received, July 7th*, 1958.]

112. *Chemistry of Hop Constituents. Part XIII.* The Hydrogenation of* isoHumulone.

By P. Margaret Brown, G. A. Howard, and A. R. Tatchell.

*iso*Humulone A and *iso*cohumulone A are hydrogenated in acetic acid over Adams catalyst to the corresponding tetrahydro-derivatives. Similar compounds are obtained by alkaline isomerisation of tetrahydrohumulone and tetrahydrocohumulone. Hydrogenation over the same catalyst in alkaline solution affords dihydro-derivatives, whereas in methanol solution other hydro-compounds are formed.

The conversion of humulone (I; R = CH_2Pr^i) into bittering substances such as occur in beer is a complex change, for several "*iso*humulones" are known while their characterisation is as yet incomplete and their inter-relations obscure.[1] Windisch *et al.*[2] suggested that humulone was converted in aqueous solution at differing pH levels into an inseparable mixture of "*iso*humulone" (now termed "*iso*humulone A"[1]), $C_{21}H_{30}O_5$, and "resin B", $C_{17}H_{20}O_5$, which were formulated on the basis of earlier work by Wieland[3] as (II) and



(III), respectively. This hypothesis appeared to be confirmed by the finding by Govaert and Verzele[4] that catalytic reduction of the supposed mixture under unspecified conditions afforded the corresponding tetrahydro*iso*humulone, m. p. 43° (equivalent weight 366), and the dihydro-derivative, m. p. 65° (equivalent weight 310), of "resin B", which were separated by chromatography. The latter compound was said to give dihydrohumulinic acid (IV) on oxidation with hypoiodite and both gave this acid on alkaline hydrolysis. Carson[5] subsequently isolated from the products resulting from treating humulone in alcoholic alkali a series of "*iso*humulones," some of which were crystalline (as distinct from earlier oily products). The existence of these products was subsequently confirmed and a system of nomenclature suggested to distinguish between them.[1] Hydrogenation of the crystalline *iso*humulones now designated B and C in methanol over palladised charcoal gave two different dihydro-derivatives, of high melting point, which were both hydrolysed by alkali to dihydrohumulinic acid, acetone, and *iso*butyraldehyde.[5] Since the hydrogenation of *iso*humulone thus appeared to offer a means both of detecting heterogeneity and of characterisation its effects have been investigated.

Conditions closely parallel to those used by Windisch *et al.*[2] have been used regularly in the present studies to prepare *iso*humulone A without any evidence for the presence of resin B emerging. It was accordingly interesting to find that the hydrogenation of the product in methanol over palladised charcoal appeared at first, on the basis of solubility in benzene, to give two amorphous products identical in light absorption but softening at about 40° and 60° respectively and thus apparently comparable with the materials reported by Govaert and Verzele. Counter-current distribution, however, indicated that both had the same compound as the major constituent, and alkaline hydrolysis of each gave the same products in good yield: the reality of "resin B" as a separate entity is accordingly open

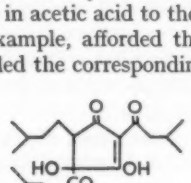
* Part XII, *J.*, 1958, 1460.

[1] Howard, Slater, and Tatchell, *J. Inst. Brewing*, 1957, 237.
[2] Windisch, Kohlbach, and Schleicher, *Woch. Brau.*, 1927, **44**, 453 *et seq.*
[3] Wieland, *Ber.*, 1925, **58**, 2012.
[4] Govaert and Verzele, *Congr. int. Industr. Ferm.*, 1947, 297.
[5] Carson, *J. Amer. Chem. Soc.*, 1952, **74**, 4615.

to doubt. In agreement with these results, chromatography of the material on silica gel, followed by distillation in a vacuum, gave a tetrahydro*iso*humulone, $C_{21}H_{34}O_5$, m. p. 32—34°, which counter-current distribution showed to be homogeneous. Catalytic hydrogenation of *iso*humulone A in acetic acid over Adams catalyst afforded a compound with identical physical properties and at present this provides the most convenient method of preparation. The compound was optically active, the magnitude of the rotation depending upon the pH, as in the case of humulone. The infrared and the ultraviolet light absorption, the hydrolysis to dihydrohumulinic and γ-methylvaleric acid, and the inability to take up iodine were consistent with its formulation as (V).

Now, tetrahydrohumulone can be prepared by the hydrogenolysis of lupulone [6] and is hydrolysed by alkali to dihydrohumulinic and γ-methylvaleric acid. It was found that under controlled alkaline conditions tetrahydrohumulone is isomerised, though more slowly than humulone itself. The product was clearly a tetrahydro*iso*humulone and had the same light absorption and partition properties as that prepared from *iso*humulone A. It differed from that product, however, in having little or no optical activity, as would be expected from its origin, and also in having a higher melting point (49—53°, as compared with 32—34°). A similar situation arose with the case of the tetrahydro-derivatives of *iso*cohumulone. (−)-Cohumulone was converted by alkali into a dextrorotatory *iso*-cohumulone A [1] which was smoothly reduced in acetic acid over Adams catalyst to a tetrahydro*iso*cohumulone, $C_{20}H_{32}O_5$, m. p. 40—46°, $K = 0{\cdot}47$ on counter-current distribution. Isomerisation in aqueous alkali of the (±)-tetrahydrocohumulone prepared from colupulone [7] afforded a tetrahydro*iso*cohumulone with the same partition coefficient but a melting point of 55—58°, whilst an analogous preparation in which alcoholic alkali was used gave a product with again the same partition coefficient and melting at 50—52°. The absorption spectra of the various tetrahydro*iso*-compounds were compared, with the object of ascertaining whether these differences in melting point were of stereochemical origin, for Carson [5] reported small but significant differences between the light absorption properties of the *iso*humulones B, C, and D. The samples of tetrahydro*iso*humulone prepared from (−)-humulone and synthetic lupulone had very similar absorption spectra, and this was true also of the corresponding *iso*cohumulone derivatives. The significance of the differences between the pairs of spectra is not easily assessed, but the close similarity both here and with the partition coefficients, suggests that the differences in melting points are due merely to the racemic or optically active nature of the compounds.

The tetrahydro*iso*-compounds, irrespective of their origin, were oxidised by bismuth oxide in acetic acid to the corresponding acyl*cyclo*pentanetriones: tetrahydro*iso*humulone, for example, afforded the *iso*humulinic acid (VI). Similar oxidation of *iso*humulone A afforded the corresponding compound (VII) which had previously been prepared by other



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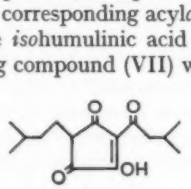

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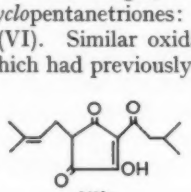

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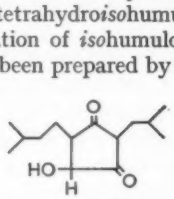


(VIII)

routes.[8] The specificity of this oxidative reagent has not been closely investigated but, as it is said to affect the CO·CH·OH group,[9] it presumably also attacks the grouping CO·C(OH)·CO. On this assumption the isolation of the above oxidation products provides new evidence for the formulation of the *iso*-compounds and their reduction products as diacylhydroxy*cyclo*pentanediones.

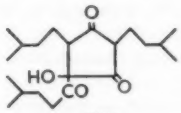
The hydrogenation of *iso*humulone A in methanol over Adams catalyst differed from

[6] Wöllmer, *Ber.*, 1925, **58**, 672.
[7] Howard, Pollock, and Tatchell, *J.*, 1955, 174.
[8] Howard and Slater, *J.*, 1957, 1924.
[9] Rigby, *J.*, 1951, 793.

that in acetic acid, the product being an oil, $C_{21}H_{38}O_4$ or $C_{21}H_{36}O_4$, containing one oxygen atom less than the starting material. No crystalline derivatives could be obtained and the compound, designated here *neo*hydro*iso*humulone, was stable to alkali and gave no volatile products on ozonolysis. A compound with the same properties was formed similarly from tetrahydro*iso*humulone. In acidic methanol it had $\lambda_{max.}$ 253 mμ (ε 11,800) and in alkaline methanol $\lambda_{max.}$ 274 mμ (ε 17,200). This light absorption is virtually identical with that of a compound, $C_{14}H_{24}O_3$, obtained by the hydrogenation of co-humulinic acid, $C_{14}H_{20}O_4$. The latter reduction product failed to give *iso*butyric acid on oxidation [10] and its infrared absorption was consistent with the presence of free hydroxyl, enolic hydroxyl, and conjugated carbonyl groups, but there was no absorption due to a free carbonyl group. It is accordingly formulated as (VIII). The light absorption of *neo*hydro*iso*humulone suggests that it also is a substituted *cyclo*pentane-1 : 3-dione, since compounds of this type have maximal light absorption at 240—250 mμ in acidic media and at about 270 mμ in the enol form,[11,12] whereas 2-acyl*cyclo*alkanones absorb at longer wavelengths,[12] *e.g.*, 2-acetyl*cyclo*pentanone has $\lambda_{max.}$ 285 mμ (ε 7500) in acidic and $\lambda_{max.}$ 305 mμ (ε 19,800) in alkaline ethanol.

Oxidation of *neo*hydro*iso*humulone by hot alkaline hydrogen peroxide gave *ca.* two equivalents of γ-methylvaleric acid and no *iso*valeric acid. Further, the corresponding *neo*hydro*iso*cohumulone reduced two mols. of periodate to give material which gave γ-methyl-valeric acid but neither *iso*butyl nor *iso*hexyl methyl ketone on hydrolysis. These results, together with the light absorption properties, suggest that the *neo*hydro*iso*-compounds are to be formulated as (IX) or (X). The infrared absorption was similar to that of compound (VIII), except for the indicated presence of a free carbonyl group, the absorption due to free hydroxyl being relatively weaker than was the case with (VIII). Structure (IX) is therefore proposed for *neo*hydro*iso*humulone. It is to be noted, however, that although *neo*hydro*iso*humulone, like (VIII), failed to form a copper complex it had three active hydrogen atoms. It is, on the other hand, not uncommon in this field for active hydrogen analyses to give unexpected results. The hydrogenation of *iso*cohumulone A or its tetrahydro-derivative in methanol likewise affords a corresponding *neo*hydro*iso*-cohumulone, and the ultraviolet light absorption of its reduction product suggests that *iso*humulone C behaves likewise.

It is noteworthy that, whereas *iso*humulone A afforded a tetrahydro-derivative, the isomers B and C gave only dihydro-compounds under apparently similar conditions of hydrogenation.[5] Since the latter substances had high melting points, further attempts to prepare a dihydro*iso*humulone A were made. The difference between the course of hydrogenation of *iso*humulone A in neutral and acidic solvents prompted an investigation into its behaviour in alkaline solution. Over Adams catalyst in aqueous sodium carbonate it afforded a resinous product different from both tetrahydro- and *neo*hydro-*iso*humulone. Its empirical formula, $C_{21}H_{32}O_5$, iodine value, and light absorption in both the ultraviolet



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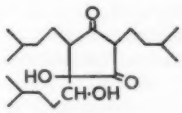

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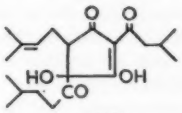

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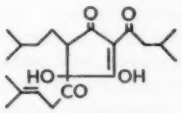

(XII)

and the infrared region all suggest that it was a dihydro-derivative, (XI) or (XII), of *iso*humulone. The isolation of humulinic acid after alkaline hydrolysis provides some support for the former structure, but little reliance can be placed on this because of the low yield. No additional reliable confirmatory evidence could be obtained and, in view of the non-crystalline nature of the material, it was not investigated further.

[10] Howard and Tatchell, *J.*, 1954, 2400.
[11] Howard and Pollock, *J.*, 1952, 1902.
[12] Eistert and Weiss, *Chem. Ber.*, 1954, **87**, 108.

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Experimental

Hydrogenation of iso*Humulone A.*—(*a*) *iso*Humulone A (853 mg.) was hydrogenated in methanol (70 ml.) over Adams catalyst (100 mg.). That part of the crude product which was extractable from ether by aqueous sodium carbonate was isolated in the usual way and distilled at 130° (bath)/2 × 10^{-3} mm., to give neo*hydroiso*humulone (Found: C, 71·2; H, 10·5; active H, 0·83. $C_{21}H_{36}O_4$ requires C, 71·6; H, 10·2; 3 active H, 0·85%), $\lambda_{max.}$ 253 mμ (ε 11,800) in acidic ethanol and 274 mμ (ε 17,200) in alkaline ethanol. The reduction product tasted bitter, gave no copper complex soluble in chloroform, failed to reduce Fehling's solution, gave a positive iodoform reaction, and was unaffected by boiling N-ethanolic alkali or by potassium hydrogen sulphate in boiling toluene. A trace (0·06 mol.) of acetone was produced by ozonolysis. Attempts to prepare an oxime, semicarbazone, 2 : 4-dinitrophenylhydrazone, or benzoate failed to give crystalline products.

Similar hydrogenations of two crystalline *iso*humulones (m. p. 123—124°, $[\alpha]_D$ −15·7° in methanol; m. p. 129—130°, $[\alpha]_D$ −40·6° in methanol) gave products which failed to distil at 135°/10^{-4} mm., but had ultraviolet light absorption identical with that of *neo*hydroiso-humulone.

(*b*) A solution of the compound (617 mg.) in acetic acid (20 ml.) was hydrogenated over Adams catalyst. A portion of the product (580 mg.) was analysed by counter-current distribution which showed it to be mainly (70%) tetrahydro*iso*humulone, and the remainder afforded this compound (m. p. 31—33°) on distillation *in vacuo*.

(*c*) A solution of the compound (616 mg.) in methanol (5 ml.) and aqueous 2N-sodium carbonate (50 ml.) was hydrogenated over Adams catalyst, the product chromatographed on silica gel, and the portion eluted by benzene (375 mg.) distilled, to give *dihydroisohumulone A* as an oil (Found: C, 69·1; H, 9·1. $C_{21}H_{32}O_5$ requires C, 69·2; H, 8·8%), $\lambda_{max.}$ 225 and 274 mμ ($E^{1\%}_{1\,cm.}$ 310 and 256) in acidic ethanol and 252 and 272 (inflexion) mμ ($E^{1\%}_{1\,cm.}$ 405 and 350) in alkaline ethanol, and iodine value 72. This gave a brown colour with ferric chloride in methanol; attempts to hydrolyse it with aqueous-ethanolic alkali failed to give recognisable products, except a volatile acid isolated in low yield and considered to be γ-methylvaleric acid (gas chromatography).

(*d*) Hydrogenation in methanol over palladium–charcoal gave a product with ultraviolet light absorption like that of *iso*humulone or its di- or tetra-hydro-derivative. Trituration with benzene gave a soluble and an insoluble fraction in the proportions 2 : 1. Alkaline hydrolysis of either fraction afforded dihydrohumulinic and γ-methylvaleric acid (70—80% yield in each case), the former identified by m. p. and mixed m. p., and the latter as the *p*-bromophenacyl ester and by gas chromatography. The fraction soluble in benzene had 71% of material having a partition coefficient identical with that of tetrahydro*iso*humulone when examined by counter-current distribution. A similar analysis of the fraction insoluble in benzene indicated the presence of 50% of tetrahydro*iso*humulone. Chromatography on silica gel of the portion soluble in benzene afforded material eluted by benzene, which distilled at 125° (bath)/10^{-5} mm. to give *tetrahydroisohumulone*, m. p. 32—34° (Found: C, 69·1; H, 9·1. $C_{21}H_{34}O_5$ requires C, 68·8; H, 9·3%), $[\alpha]_D$ +24·5° in neutral methanol, $[\alpha]_D$ +98° in alkaline methanol, $\lambda_{max.}$ 230 and 275 mμ ($E^{1\%}_{1\,cm.}$ 250 and 250) in acidic ethanol and 253 mμ ($E^{1\%}_{1\,cm.}$ 456) in alkaline ethanol. Hydrogenation in methanol over Adams catalyst afforded a product identical in ultraviolet absorption with *neo*hydro*iso*humulone.

Tetrahydro*iso*humulone had a partition coefficient 1·04 in the system 2-methylheptane–phosphate buffer (0·5M; pH 6·5).

Hydrogenation of Dihydroisohumulone.—In methanol over Adams catalyst this afforded a product with the ultraviolet light absorption of *neo*hydro*iso*humulone. Reduction over Adams catalyst in acetic acid afforded an oil which distilled at 120°/5 × 10^{-4} mm., to give a *product* whose infrared absorption and counter-current distribution were unlike those of tetrahydro*iso*humulone although the two compounds had similar ultraviolet absorption (Found: C, 71·4; H, 10·5. $C_{21}H_{36}O_4$ requires C, 71·6; H, 10·2%).

Hydrogenation of iso*Cohumulone A.*—Hydrogenation of *iso*cohumulone A (892 mg.) in acetic acid (30 ml.) over Adams catalyst afforded a low-melting solid, which was purified by elution from silica gel with benzene (85% recovery) and finally by distillation at 145° (bath)/10^{-3} mm., to give *tetrahydroisocohumulone*, m. p. 40—46° (Found: C, 67·8; H, 9·4. $C_{20}H_{32}O_5$ requires C, 68·2; H, 9·1%). It had $[\alpha]_D$ +28° in methanol, and +89° in alkaline methanol, a

partition coefficient of 0·47 between 2-methylheptane and phosphate buffer (pH 6·5), and $\lambda_{max.}$ 230 and 273 mμ ($E^{1\%}_{1\,cm.}$ 294 and 274) in acidic ethanol and 253 mμ ($E^{1\%}_{1\,cm.}$ 515) in alkaline ethanol.

(±)-*Tetrahydroisocohumulone*.—(*a*) A solution of (±)-tetrahydrocohumulone [10] (480 mg.) in aqueous N/15-sodium hydroxide (74 ml.) was heated under reflux under nitrogen for 9 min. The product was isolated in the usual way and purified by chromatography on silica gel. The material eluted by benzene had m. p. 53—54° and afforded tetrahydro*iso*cohumulone, m. p. 55—58°, on distillation at 105° (bath)/10^{-5} mm. (Found: C, 68·4; H, 8·9%). It had a partition coefficient (cf. above) of 0·46, $[\alpha]_D$ +6° in both neutral and alkaline ethanol, and $\lambda_{max.}$ 230 and 273 mμ ($E^{1\%}_{1\,cm.}$ 264 and 284) in acidic ethanol and $\lambda_{max.}$ 253 mμ ($E^{1\%}_{1\,cm.}$ 494) in alkaline ethanol.

(*b*) (±)-Tetrahydrocohumulone (2·86 g.) was isomerised in ethanolic alkali as described for humulone by Carson; [5] the product (2·53 g.) crystallised and 70% of it had the same partition coefficient as tetrahydro*iso*cohumulone in the usual system. Chromatography on silica gel followed by distillation at 128° (bath)/10^{-3} mm. afforded tetrahydro*iso*cohumulone, m. p. and mixed m. p. 50—52°, $\lambda_{max.}$ 230 and 273 mμ ($E^{1\%}_{1\,cm.}$ 260 and 250) in acidic and 253 mμ ($E^{1\%}_{1\,cm.}$ 574) in alkaline ethanol (Found: C, 68·4; H, 9·4%).

(±)-*Tetrahydroisohumulone*.—A solution of tetrahydrohumulone (668 mg.) in aqueous N/15-sodium hydroxide (100 ml.) was boiled under reflux under nitrogen for 9 min. The product was isolated and purified by chromatography on silica gel as was tetrahydro*iso*cohumulone, and then distilled at 110° (bath)/10^{-5} mm., to give *tetrahydroisohumulone*, m. p. 49—53°, $[\alpha]_D$ −2° in neutral and +13° in alkaline methanol, $K = 1·04$ between 2-methylheptane and phosphate buffer (pH 6·5), $\lambda_{max.}$ 230 and 275 mμ ($E^{1\%}_{1\,cm.}$ 250 and 265) in acidic and 253 mμ ($E^{1\%}_{1\,cm.}$ 480) in alkaline ethanol (Found: C, 68·5; H, 9·4. $C_{21}H_{34}O_5$ requires C, 68·8; H, 9·3%).

Alkaline Hydrolysis of Tetrahydroisohumulone.—A solution of tetrahydro*iso*humulone (478 mg.) in ethanol (3 ml.) and aqueous N-sodium hydroxide (7 ml.) was boiled under reflux under nitrogen for 3 hr. The hydrolysate was acidified and concentrated by distillation, the distillate being collected. The crystalline material (260 mg., 74%) present in the distillation residue had m. p. 122—124°, and afforded dihydrohumulinic acid, m. p. and mixed m. p. 126°, on recrystallisation from methanol. From the distillate obtained above, the acids were isolated in the usual way. Analysis by gas chromatography indicated the presence of γ-methylvaleric acid (80%), and the *p*-bromophenacyl ester, m. p. and mixed m. p. 77—78°, was obtained in 20% yield in the usual way.

Oxidation of Tetrahydroisohumulone with Bismuth Oxide.—A solution of tetrahydro*iso*humulone (200 mg.) prepared from either humulone or synthetic lupulone, in acetic acid (10 ml.), was boiled under reflux with bismuth trioxide (450 mg.) for 5 hr. A yellow solid (181 mg.) was extracted from the acidified solution by ether after dilution with water. Recrystallisation from light petroleum (b. p. 40—60°) afforded *iso*humulinic acid, m. p. and mixed m. p. 142—143° (oxime, m. p. and mixed m. p. 208°). The product gave the same colour (blue-purple) with methanolic ferric chloride and had the same ultraviolet light absorption as *iso*humulinic acid. Tetrahydro*iso*humulone was recovered unchanged when boiled with acetic acid alone.

Oxidation of Tetrahydroisocohumulone with Bismuth Oxide.—A solution of tetrahydro*iso*cohumulone (286 mg.), prepared from either cohumulone or colupulone, in acetic acid (6 ml.) was boiled with bismuth oxide (450 mg.) for 4 hr. The product isolated in the usual way was *iso*cohumulinic acid (52 mg.), m. p. and mixed m. p. 121—123°.

Oxidation of iso*Humulone A by Bismuth Oxide*.—A solution of *iso*humulone A (298 mg.) in acetic acid (6 ml.) was boiled under reflux with bismuth oxide (450 mg.) for 1 hr., longer boiling causing extensive decomposition. The solution was acidified with hydrochloric acid, diluted with water, and extracted with ether. The extract was washed with water, dried, and evaporated and the residue recrystallised from light petroleum, thus giving a product (2·5 mg.), m. p. 131—133° unchanged when mixed with 5-(3-methylbut-2-enyl)-3-*iso*valeryl*cyclo*pentane-1 : 2 : 4-trione.

Oxidation of neo*Hydroisohumulone by Alkaline Hydrogen Peroxide*.—A solution of *neo*hydro-*iso*humulone (500 mg.) in aqueous 2N-sodium hydroxide (14 ml.) was boiled under reflux and 30% hydrogen peroxide (5 ml.) was added; similar additions were made at hourly intervals for 3 hr. After 4 hr. the solution was acidified at 0° and extracted with ether, and the acids were extracted with aqueous sodium hydrogen carbonate, then recovered as an oil (370 mg.) which afforded *p*-bromophenacyl γ-methylvalerate, m. p. and mixed m. p. 75—77°.

In a similar experiment, 98% of the oxidation product was soluble in aqueous sodium

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hydrogen carbonate, and examination of it by gas chromatography using an internal standard showed that 73% of it was a mixture of *iso*valeric, γ-methylvaleric, and a C_7 acid in the ratios 6 : 78 : 17. A portion of the material soluble in aqueous sodium hydrogen carbonate was distilled with steam, the non-volatile acids were again oxidised by hydrogen peroxide in boiling alkali, and the material soluble in aqueous sodium hydrogen carbonate was isolated. This then contained 22% of γ-methylvaleric acid Thus the oxidation of *neo*hydro*iso*humulone finally afforded *ca.* 1·9 mol. of γ-methylvaleric acid. The acidic product which was not volatile with steam had $\lambda_{max.}$ 230 mμ in acidic, and 263 mμ in alkaline, ethanol but did not crystallise.

Hydrogenation of iso*Humulone.*—Humulone (6·37 g.) was isomerised by Carson's method, and the product diluted with light petroleum, thus affording crystalline material (729 mg., 15%) which was recrystallised successively from light petroleum, methanol, and light petroleum to give "*iso*humulone," m. p. 124—125°, $[\alpha]_D$ +10·4° and +56° in neutral and alkaline methanol respectively (Found: C, 69·7; H, 8·45. Calc. for $C_{21}H_{30}O_5$: C, 69·6; H, 8·2%). Counter-current distribution with 2-methylheptane and phosphate–citrate buffer (pH 5·0) indicated the presence of one major component with K 1·42, together with minor components. The residue remaining after the original removal of crystalline "*iso*humulone" was dissolved in ether and shaken with aqueous 2N-sodium hydroxide, and the insoluble sodium salt was removed. The oily *iso*humulone then obtained (3·8 g.) consisted primarily (75%) of *iso*humulone A as judged by counter-current distribution. A portion (978 mg., $[\alpha]_D$ +27·5° in methanol) was hydrogenated over Adams catalyst in acetic acid, 2 mols. of hydrogen being absorbed, to give a product (915 mg., $[\alpha]_D$ +7° in methanol) of which 60% was tetrahydro*iso*humulone as judged by its behaviour on counter-current distribution. Chromatography on silica gel gave material eluted by benzene (87% of original sample) which partially crystallised. The crystalline material was recrystallised from light petroleum to give a product, m. p. 152—154°. The non-crystalline product distilled at 128° (bath)/10^{-3} mm., had $[\alpha]_D$ +20° in neutral and +90° in alkaline methanol, $\lambda_{max.}$ 230 and 275 mμ ($E^{1\%}_{1\,cm.}$ 240 and 255) in acidic and 253 mμ ($E^{1\%}_{1\,cm.}$ 466) in alkaline ethanol and also, although not crystalline, gave analyses correct for tetrahydro*iso*humulone (Found: C, 68·8; H, 9·5. Calc. for $C_{21}H_{34}O_5$: C, 68·8; H, 9·3%).

Periodate Oxidation of neo*Hydro*iso*cohumulone.*—To a solution of *neo*hydro*iso*cohumulone (867 mg.) in ethanol (20 ml.) was added one of sodium metaperiodate (1·2 g.) in water (20 ml.), and the mixture set aside overnight. Sodium iodate was filtered off and washed with ethanol, and the combined filtrates and washings were acidified, saturated with sodium chloride, and extracted with ether. The extract was washed with brine, evaporated to low bulk, and then boiled under reflux for 2 hr. with aqueous 2N-sodium hydroxide (20 ml.). The cooled hydrolysate was extracted with ether, and the extract washed with brine, dried, and evaporated cautiously. The residue was treated with alcoholic 2 : 4-dinitrophenylhydrazine hydrochloride, and the resulting hydrazones examined chromatographically in alumina. No evidence could be obtained of the presence of ketones of low molecular weight. The alkaline solution remaining after the hydrolysis was acidified and distilled with steam. Extraction of the distillate with ether in the usual way afforded γ-methylvaleric acid (260 mg. of impure material), characterised by gas chromatography and as the *p*-bromophenacyl ester, m. p. and mixed m. p. 78°.

Infrared Spectra.—*neo*Hydro*iso*cohumulone, as a film, had absorption peaks at 2·90 (m), 3·1 to 3·4 (m), 3·4 (s), 3·8 (m), 5·85 (s), 6·1 to 6·5 (s), 6·85 (s), 7·25 and 7·35 (s), 8·0 (s), 8·57 (m), 8·85 (m), 9·22 (m), 9·4 (m), 10·3 (w), 10·85 (w), 11·8 to 12·3 (w), and 12·9 (w) μ.

Dihydro*iso*humulone, as a film, had absorption peaks at 2·85 (m), 3·35 (s), 3·7 (w), 5·85 (s), 6·1 to 6·4 (s), 6·8 and 6·9 (s), 7·2 and 7·3 (s), 7·8 (m), 8·15 (m), 8·55 (m), 9·1 to 9·3 (m), 10·15 (w) 10·40 (w), 10·8 (w), and 11·9 (w) μ.

Tetrahydro*iso*humulone, as a film, had absorption peaks at 2·85 (m), 3·35 (s), 3·7 (w), 5·85 (s), 6·1 to 6·35 (s), 6·8 (s), 7·3 (s), 7·55 (m), 7·85 (m), 8·2 (m), 8·55 (s), 8·8 (s), 10·85 (m), and 12·0 (w) μ. Tetrahydro*iso*humulone in carbon disulphide gave a similar spectrum, but with additional shoulders at 3·41, 5·75, and 7·15 μ. In carbon tetrachloride solution, distinct peaks were observable at 6·15 and 6·32 μ with shoulders at 6·60 and 6·95 μ. The spectra of samples derived from (−)-humulone and synthetic lupulone were very similar. Samples of tetrahydro*iso*cohumulone derived from (−)-cohumulone or colupulone had very similar absorption spectra when examined as films or dissolved in carbon disulphide or carbon tetrachloride and differed from the tetrahydro*iso*humulone samples chiefly in that the bands at 7·85 and 8·2 μ were absent and there was a strong band at 9·15 μ.

2-*iso*Butyl-4-hydroxy-5-*iso*pentyl*cyclo*pentane-1 : 3-dione (VIII) in Nujol had significant

absorption peaks at 2·92 (m), 3·8 (s), 6·45 (s), 7·2 (s), 7·45 (s), 7·6 (s), 7·85 (m), 8·07 (m), 8·85 (m), 9·44 (m), 10·1 (m), 11·8 (m), and 12·95 (m) μ.

The spectra were determined with a Perkin-Elmer spectrophotometer Model 137.

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113. *The Organic Chemistry of the Transition Elements. Part I. Tricarbonylchromium Derivatives of Aromatic Compounds.*

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Many aromatic compounds, ArH, displace carbon monoxide from chromium hexacarbonyl with the formation of complexes $Cr(CO)_3(ArH)$ (I). These are stable and may carry any of several functional groups. The effects of the metallic residue upon typical properties of these groups and of the aromatic system as a whole are outlined, and methods for the regeneration of the aromatic components are described.

TRICARBONYLBENZENECHROMIUM (I) was first obtained by Fischer and Ofele [1] in 27% yield from chromium hexacarbonyl and dibenzenechromium in benzene in a sealed system at 220°. We had independently discovered a simpler and more general method for preparing compounds of this type which involves heating chromium hexacarbonyl under reflux in an excess of the aromatic compound or with a molar quantity in an inert solvent.

(I) (II)

Shortly after our preliminary communication,[2] Natta and his co-workers also described [3] the direct preparation of several of these compounds, but used a pressurised system (with intermittent release of carbon monoxide) and higher temperatures (200—235°). The work of Fischer and his school [1] shows that equilibria are involved in these reactions—an excess of carbon monoxide converts the dibenzenechromium complex into the hexacarbonyl—and therefore it is advantageous in principle, as well as much easier in practice, to employ an open system, the free escape of carbon monoxide then driving the reaction to completion.

In early experiments decalin was employed as solvent, but because the commercial product contains tetralin as an impurity, and perhaps because of hydrogen-transfer processes, products containing the tricarbonylchromium complex of tetralin were often obtained. Since the final product has a considerable dipole moment and is formed from more or less non-polar components, the reaction should be facilitated by the use of a polar solvent. Of the many tried, diethylene glycol dimethyl ether was the most suitable. Its use made possible the direct preparation of the parent member of the series, tricarbonylbenzenechromium, and also greatly improved the yields of other complexes. A list of complexes, $(ArH)Cr(CO)_3$, is given in Table 1; all are stable, yellow or orange, and crystalline; all gave correct analyses for carbon and hydrogen, and in one case for oxygen.

The rate of formation of these complexes is of obvious interest. The conversion of an aromatic compound into such a complex results ultimately in approximately equal bonding to all six aromatic carbon atoms, and although it can, and should, be regarded as an

[1] Fischer and Ofele, *Angew. Chem.*, 1957, **69**, 715; *Chem. Ber.*, 1957, **90**, 2532.
[2] Nicholls and Whiting, *Proc. Chem. Soc.*, 1958, 152.
[3] Natta, Ercoli, and Calderazzo, *Chim. e Ind.*, 1958, **40**, 287.

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electrophilic attack on the aromatic system it cannot be grouped either with typical attacks on single carbon atoms giving σ-complexes as intermediates (nitration, etc.), or with attacks on individual double bonds giving initially one-bond π-complexes (formation of silver complexes, ozonolysis, dihydro-diol formation). The qualitative experiments already made show that electronic effects roughly parallel those observed in nitration studies, the reaction being facilitated by electron-repelling substituents, *e.g.*, NMe_2 and retarded by electron-attracting groups, *e.g.*, Cl and CO_2Me. A second important factor is the steric effect of substituent groups. Thus the rate sequence $o \sim m > p$ was always observed with disubstituted benzenes, while *tert.*-butylbenzene reacted much more slowly than toluene. The latter result tends to disprove the rate-determining formation of a one-bond π-complex (II), followed by intramolecular displacement of carbon monoxide, since in that case the reactivity of the molecule would depend only upon the environment of its most reactive C–C bond. [The possibility that complex (II) is formed rapidly and reversibly and that its transformation into (I) by intramolecular displacement of carbon monoxide is the rate-

TABLE 1. *Direct preparation of tricarbonyl(arene)chromium compounds.*

					Analysis			
					Found (%)		Calc. (%)	
Aromatic compound	Method	Time (hr.)	Yield (%)	M. p.	C	H	C	H
Benzene	C	9·0	30	165·5—166·5°	50·3	3·2	50·45	2·8
Toluene	A	12·0	10	82·5—83·5	52·2	3·6	52·6	3·5
	C	5·0	80					
o-Xylene	A	6·0	81	90—91·4	54·5	4·4	54·5	4·15
m-Xylene	A	6·0	27	107—108·5	54·35	4·1	54·5	4·15
p-Xylene	A	3·0	20	99—100	53·95	4·4	54·5	4·15
	A	16·0	87					
Mesitylene *	A	3·8	84	177—178	57·1	4·9	56·25	4·7
Hexamethylbenzene	C	4·0	51	211—213 (dec.)	60·4	6·2	60·4	6·05
Tetralin	A	3·0	85	116—117·5	58·3	4·65	58·2	4·5
Anisole	A	6·0	94	86—87	49·5	3·5	49·2	3·3
Methyl *o*-tolyl ether	A	3·0	99	75—77	51·45	3·85	51·15	3·9
Methyl *p*-tolyl ether	A	4·5	70	52—53·5	51·2	4·05	51·15	3·9
Aniline	B	3·0	91	173—175 (dec.)	46·8	3·2	47·15	3·05
o-Toluidine	B	1·5	98	130—131·8	49·65	3·65	49·4	3·7
m-Toluidine	B	1·5	97	137—138·7	49·4	3·65	49·4	3·7
p-Toluidine	B	8·0	46	156—157·5	49·4	3·7	49·4	3·7
N-Methylaniline	B	3·0	88	122·5—124	49·65	3·7	49·4	3·7
NN-Dimethylaniline	B	3·0	91	145·8—146·5	51·3	4·35	51·35	4·3
NN-Dimethyl-*o*-toluidine	B	3·0	99	76·5—78	52·7	4·55	53·1	4·75
Methyl benzoate	A	4·5	72	97·5—98·5	48·3	3·1	48·55	2·95
Ethyl phenylacetate	B	2·5	88	oil	—	—	—	—
Fluorobenzene	C	3·0	23	122·5—124	46·6	2·5	46·55	2·15
Chlorobenzene	C	3·0	52	102—103	—	—	—	—
Benzyl alcohol	A	3·0	54	95·5—96·5	49·1	3·2	49·2	3·3
Acetophenone	C	4·5	35	91—92·5	51·5	3·25	51·55	3·1
tert.-Butylbenzene	A	6·0	5	83·5—84·5	57·7	5·2	57·75	5·2
				Molybdenum complex				
Mesitylene	B	3·0	70	150 (dec.)	48·15	4·15	48·0	4·0

Method: A, Aromatic compound as solvent. B, Decalin as solvent. C, Diethylene glycol dimethyl ether as solvent.

* Found: O, 18·1. Calc.: O, 18·7%.

determining step is not thereby excluded, but seems most unlikely.] The observed rate sequence is consistent with participation of the aromatic sextet as a whole in the rate-determining stage, since any transition state involving this and chromium hexacarbonyl would suffer more interference from *para*- than from *ortho*- or *meta*-substituents.

Limitations to the reaction were encountered in the presence of certain functional groups (CO_2H, CHO, CN, and NO_2); the chromium hexacarbonyl then suffered decomposition before the complex-forming reaction became appreciable. The complexes

derived from phenol and quinol were very readily oxidised and so could not be easily purified.

The characteristic properties of functional substituents are largely preserved in these complexes. Thus, the unstable tricarbonylphenolchromium can be methylated and acetylated to the anisole and phenyl acetate analogues and the aniline complex converted into the corresponding acetanilide derivative. This makes possible the preparation of some otherwise inaccessible complexes, such as those of benzoic and phenylacetic acid, which were prepared by alkaline hydrolysis of the corresponding esters. However, attempts to prepare the nitrobenzene complex by oxidation of the aniline analogue with peroxytrifluoroacetic acid were unsuccessful, the reagent disrupting the molecule, probably by first oxidising the chromium atom (cf. the behaviour of ferrocene [4]). Similarly the attempted indirect synthesis of tricarbonylbenzonitrilechromium failed, owing to our inability to prepare the analogous amide from the benzoic acid complex by using thionyl chloride and ammonia or from the methyl ester and alcoholic ammonia. Both molecules were disrupted, although from the latter reaction a small amount of tricarbonyl(benzoic acid)chromium could be isolated. Methylation of the aniline complex by methyl iodide and sodium carbonate stopped at the monosubstituted stage.

The aromatic tricarbonylchromium complexes are recovered unchanged, provided the molecule contains no reducible function, after treatment with sodium ethoxide in boiling ethanol or with lithium aluminium hydride at temperatures up to 30°. By using the latter reagent tricarbonyl(benzyl alcohol)chromium, identical with the product from benzyl alcohol and chromium hexacarbonyl, was prepared in high yield from the methyl benzoate complex.

Without exception, all the oxidising agents examined attacked the tricarbonylchromium residue with evolution of gas and generation of tervalent chromium. For example, manganese dioxide instantly destroyed the benzyl alcohol complex and then slowly oxidised the liberated benzyl alcohol to benzaldehyde. Similar observations were made in the attempted permanganate oxidation of the toluene complex and diazotisation of the aniline derivative.

In ferrocene, the electrons involved in the bonding between the hydrocarbon residue and the metal atom show mobility characteristic of aromatic or conjugated ethylenic systems. Although easily oxidised by nitric acid, bromine, etc., ferrocene readily undergoes Friedel–Crafts acylation. Dibenzenechromium is not substituted under similar conditions, although its much lower stability precludes more drastic treatment.[5] The tricarbonylchromium derivatives of anisole and mesitylene could, however, be heated under reflux with acetyl chloride and aluminium chloride in methylene dichloride for several hours and then recovered unchanged in 10—50% yield. This lack of reactivity toward electrophilic reagents is not unexpected, since pK_a measurements on the benzoic and phenylacetic acid derivatives (see below) show that the tricarbonylchromium π-grouping has a similar electron-withdrawing power to a *p*-nitro-group, and the inertness of nitrobenzene in Friedel–Crafts acylations is well known. The result, however, makes it unlikely that electrophilic substitution will prove useful synthetically in this field.

The presence of an electron-deficient aromatic ring in these tricarbonylchromium derivatives suggests that they might undergo nucleophilic substitution much more easily than the parent compounds. This proved so; the derivative of chlorobenzene could be converted into the anisole analogue in high yield at 65°. The synthetical use of this observation and the mechanism of substitution are now under investigation. As yet attempts to effect free-radical substitution have not proved successful.

Synthetical applications would require that the π-bound tricarbonylchromium residue could be cleanly and satisfactorily removed when desired. The oxidative methods described suffer from the disadvantage that the aromatic component may undergo further

[4] Woodward, Rosenblum, and Whiting, *J. Amer. Chem. Soc.*, 1952, **74**, 3458.
[5] Fritz and Fischer, *Z. Naturforsch.*, 1957, **12***b*, 67.

transformation. Thermal decomposition of the toluene complex proceeds smoothly at about 200°, giving a mixture of toluene (76%), chromium hexacarbonyl (67%), and pyrophoric chromium. For many purposes it would, however, be preferable to displace the aromatic component by attack on chromium with a more powerful ligand. Displacement by a more nucleophilic aromatic ring does not proceed to a measurable extent, the toluene complex being recovered after prolonged treatment with boiling dimethylaniline or mesitylene. Electron donors such as pyridine, dimethylphenylarsine, and triphenylphosphine, on the other hand, were very efficient and both the aromatic component and the *p*-complex could be isolated. The nature of these and other *p*-complexes will be dealt with in greater detail in a subsequent paper.

The dissociation constants of ferrocenecarboxylic acids are comparable with those of typical aliphatic or aromatic acids,[4] and a carbon atom bonded to a transition-metal atom by an electron system of this type may thus be comparable in electronegativity with one bonded by sp^3 or sp^2 electrons to carbon and hydrogen atoms. Unfortunately the limited range of diarenechromiums available does not include a carboxylic acid. As a first approximation of the extent of electron availability at a carbon centre in a π-tricarbonylbenzenechromium derivative and as a check on the steric effects of the π-bound tricarbonylchromium grouping, the dissociation constants of the derivatives of benzoic and phenylacetic acid were determined in 50% ethanol, along with the unsubstituted and *p*-nitro-acids (Table 2). The derivative of phenylacetic acid had the same dissociation constant as *p*-nitrophenylacetic acid, but in the benzoic acid series the organochromium acid was appreciably weaker than the *p*-nitro-acid. These results suggest that the π-bound tricarbonylchromium group withdraws electrons at least as strongly as a *p*-nitro-group (though by quite a different combination of mechanisms) and that it also exerts a steric effect, hindering solvation and weakening any process of ionisation, comparable with that of a large *ortho*-substituent.

TABLE 2. *Dissociation constants* (pK^*) *of substituted benzoic and phenylacetic acids.*

$Ph{\cdot}CO_2H$	5·68	$Ph{\cdot}CH_2{\cdot}CO_2H$	5·64
π-$Cr(CO)_3(Ph{\cdot}CO_2H)$	4·77	π-$Cr(CO)_3(Ph{\cdot}CH_2{\cdot}CO_2H)$	5·02
p-$NO_2{\cdot}C_6H_4{\cdot}CO_2H$	4·48	p-$NO_2{\cdot}C_6H_4{\cdot}CH_2{\cdot}CO_2H$	5·01

Molybdenum hexacarbonyl reacts much more rapidly than chromium hexacarbonyl with aromatic compounds to form similar derivatives $Mo(CO)_3(ArH)$. Unfortunately they are generally less stable than the chromium analogues.

[*Note Added December 3rd*, 1958.—Fischer, Öfele, Essler, Fröhlich, Mortensen, and Semmlinger (*Z. Naturforschung*, 1958, 13b, 458) have also discovered the direct synthesis of these complexes from aromatic compounds and chromium hexacarbonyl.]

EXPERIMENTAL

Only representative examples of the use of the three methods of direct preparation are given in full; for other complexes the procedure differs inappreciably, except as regards reaction time. Analytical data are given in Table 1. Unless otherwise stated, all complexes are yellow crystalline solids, stable to light and air at moderate temperatures when pure but slowly attacked under these conditions when dissolved. " Method B " is seldom, if ever, preferable to " method C "; and " method A " is of little value with compounds which boil below 120°.

Method A. Tricarbonylmesitylenechromium.—A solution of chromium hexacarbonyl (1·07 g.) in mesitylene (10 c.c.) was heated under reflux in an atmosphere of nitrogen. Chromium hexacarbonyl which sublimed was returned to the reaction mixture mechanically, until sublimation ceased (4 hr.). The deep yellow solution was cooled, diluted with ether (100 c.c.), and filtered through deactivated alumina (5 g.). Concentration to dryness afforded the *complex* (1·04 g.; 84%) as needles, m. p. 177—178°, from di*iso*propyl ether.

Method B. Tricarbonyl(NN-*dimethylaniline*)*chromium.*—A solution of chromium hexacarbonyl (2·10 g.) and dimethylaniline (4 c.c.) in decalin (20 c.c.) was heated under reflux during 3 hr. (chromium hexacarbonyl being returned mechanically), allowed to cool, and diluted with

ether (100 c.c.). The turbid solution was filtered through deactivated alumina (5 g.), the filtrate evaporated to 25 c.c., and the precipitate filtered off and thoroughly washed with light petroleum. Recrystallisation from di*iso*propyl ether furnished the *complex* (2·26 g; 91%), m. p. 145·8—146·5°.

Method C. Tricarbonyl(fluorobenzene)chromium.—The reaction solution from chromium hexacarbonyl (2·06 g.) and fluorobenzene (3 c.c.) in diethylene glycol dimethyl ether (7 c.c.) was worked up as above to yield a solid (504 mg.; 23%), m. p. 117—120°. Two recrystallisations from light petroleum gave the *complex* (321 mg.), m. p. 122·5—124°, as long needles.

Tricarbonylacetanilidechromium.—A solution of tricarbonylanilinechromium (715 mg.) and acetic anhydride (477 mg.) in pyridine (3·5 g.) was set aside overnight at room temperature in the dark. The resulting dark brown solution was poured into water (50 c.c.; at 0°) and the precipitated oil isolated with ether. Removal of solvent and crystallisation from di*iso*propyl ether–chloroform afforded the *complex* (756 mg.; 90%), m. p. 134—134·5° (Found: C, 48·4; H, 3·45. $C_{11}H_9O_4NCr$ requires C, 48·7; H, 3·3%).

Tricarbonylanisolechromium.—A solution of chromium hexacarbonyl (1·26 g.) and phenol (5 g.) in decalin (10 c.c.) was heated under reflux for 3 hr. and worked up in the usual manner to give tricarbonylphenolchromium as an unstable solid (1·20 g.). This was dissolved in aqueous potassium hydroxide (2·5 g. in 20 c.c. of water) and treated dropwise with dimethyl sulphate (7 g.). The resultant solution was heated under reflux for 2 hr. and diluted, and the organochromium complex was isolated with ether and crystallised from di*iso*propyl ether, giving the complex (1·11 g.; 87%), m. p. 86—87°, identical with that prepared directly.

Tricarbonyl(phenyl acetate)chromium.—The oil (1·01 g.) obtained from the reaction of chromium tricarbonyl (1·21 g.) with phenol (0·61 g.) in decalin (10 c.c.) during 4 hr. at 190—195° was dissolved in pyridine (5 c.c.) and acetic anhydride (2·5 g.) was added. After 16 hr. at room temperature in the dark, the mixture was diluted with water, and the product isolated with ether. Removal of solvent under reduced pressure yielded the *complex* (1·01 g.; 85% from phenol analogue), m. p. 92—95°. An analytical sample had m. p. 94—95·5° (from light petroleum) (Found: C, 49·0; H, 3·1. $C_{11}H_8O_5Cr$ requires C, 48·6; H, 2·95%).

Tricarbonyl(benzoic acid)chromium.—A solution of tricarbonyl(methyl benzoate)chromium (687 mg.; prepared directly) and potassium hydroxide (327 mg.) in water (0·5 c.c.) and methanol (20 c.c.) was kept for 16 hr. at room temperature in the dark. The mixture was diluted with water, unchanged ester was removed by ether extraction, and the aqueous layer was acidified with hydrochloric acid. Isolation with ether yielded the *complex* (617 mg.; 96%; decomp. at 194°) as orange-red clusters (from di*iso*propyl ether–chloroform) (Found: C, 46·4; H, 2·45. $C_{10}H_6O_5Cr$ requires C, 46·5; H, 2·35%).

Tricarbonyl(phenylacetic acid)chromium.—Hydrolysis of the crude ethyl phenylacetate complex (2·30 g.) with potassium hydroxide (1·0 g.) in water (1 c.c.) and methanol (20 c.c.) during 15 hr. at 17° followed by isolation in the usual manner gave the *complex* (2·03 g.; 97%), m. p. 134—135·5° (from di*iso*propyl ether) (Found: C, 48·35; H, 3·15. $C_{11}H_8O_5Cr$ requires C, 48·5; H, 3·0%).

Tricarbonyl(methyl benzoate)chromium.—A solution of tricarbonyl(benzoic acid)chromium (115 mg.) in methanol (25 c.c.) containing concentrated sulphuric acid (1 c.c.), after being kept overnight at room temperature, was poured into water, and the neutral product isolated with ether. Removal of solvent and crystallisation from light petroleum afforded the *complex* (27 mg.; 20%), m. p. 97·5—98·8°, identical with a sample prepared directly (Found: C, 49·3; H, 3·1. $C_{11}H_8O_5Cr$ requires C, 48·9; H, 3·0%).

Tricarbonyl(benzyl alcohol)chromium.—Tricarbonyl(methyl benzoate)chromium (910 mg.) in ether (10 c.c.) was cooled to −70° and treated with lithium aluminium hydride (200 mg.) in ether (10 c.c.). The solution was allowed to warm slowly to −45°; a vigorous reaction then occurred. After a few minutes the mixture was treated with ethanol (5 c.c.) and poured into dilute sulphuric acid (at 0°). Isolation with ether furnished the complex (784 mg.; 96%), m. p. 95·5—96·5°, identical with a sample prepared directly.

Reaction of Tricarbonyl(methyl benzoate)chromium with Ammonia.—A suspension of the ester complex (52 mg.) in aqueous ammonia (5 c.c.; *d* 0·88) was treated with ethanol (5 c.c.), and the mixture was heated under reflux for 12 hr. The cooled solution was diluted with water, washed with ether (2 × 20 c.c.), acidified (dilute sulphuric acid), and extracted with ether. Tricarbonyl(benzoic acid)chromium (14 mg.; 30%) was obtained; it had decomposition point 190° and was identical with a sample prepared directly.

Methylation of Tricarbonylanilinechromium.—A mixture of the amine (124 mg.), sodium carbonate (641 mg.), and methyl iodide (1 c.c.) in methanol was heated under reflux for 5 hr. Isolation in the usual manner afforded tricarbonyl(*N*-methylaniline)chromium (87 mg.; 67%), m. p. 121·5—124°, undepressed on admixture with a sample prepared directly.

Manganese Dioxide Oxidation of Tricarbonyl(benzyl alcohol)chromium.—Manganese dioxide (1·0 g.) was added portionwise to a solution of the complex (240 mg.) in methylene dichloride (25 c.c.). A vigorous evolution of gas occurred after each addition. After being stirred for 24 hr. at room temperature in the dark the solution was filtered, the solid washed well with ether, and the filtrate dried ($MgSO_4$). Solvent was removed through a Fenske column, and the pale yellow oil treated with excess of methanolic 2 : 4-dinitrophenylhydrazine reagent. The precipitate (279 mg.) in benzene–light petroleum (1 : 9) was adsorbed on deactivated alumina (50 g.). Elution with the same solvent yielded benzaldehyde 2 : 4-dinitrophenylhydrazone (131 mg.; 42%), m. p. 236—238° (from di*iso*propyl ether–light petroleum).

Attempted Acetylation of Tricarbonylmesitylenechromium.—The complex (249 mg.) in methylene dichloride (10 c.c.) was mixed with a solution of acetyl chloride–aluminium chloride in methylene dichloride (10 c.c.; 0·3 molar) and heated under reflux for 1 hr. Isolation afforded only the starting material (102 mg.), m. p. 175—176·5°.

Replacement of Chlorine by the Methoxyl Group.—Tricarbonyl(chlorobenzene)chromium (235 mg.) and sodium methoxide (from 500 mg. of sodium) in methanol (20 c.c.) were heated under reflux for 24 hr. Isolation in the usua lway yielded tricarbonylanisolechromium (207 mg.; 90%), m. p. 85·5—86·5° (from light petroleum). (Silver nitrate estimation of chloride ions liberated showed a 97% conversion.)

Thermal Decomposition of Tricarbonyltoluenechromium.—The complex (654 mg.) was slowly heated in a microdistillation unit to 200°. At about 170° chromium hexacarbonyl (219 mg.; 67%) sublimed and the liquid became very dark. At 200° toluene (197 mg.; 76%) distilled leaving a residue of metallic chromium.

Displacement Reactions with π-Complexes.—(a) *Using* NN-*dimethylaniline.* A solution of tricarbonyltoluenechromium (292 mg.) in dimethylaniline (5 c.c.) was heated under reflux for 12 hr. and allowed to cool, and the neutral product was isolated with ether. Removal of solvent furnished unchanged tricarbonyltoluenechromium (247 mg.), m. p. 82—83°.

(b) *Using dimethylphenylarsine.* A solution of tricarbonyltoluenechromium (293 mg.) in dimethylphenylarsine (1 c.c.) was maintained at 150—160° for 1 hr. Isolation gave tricarbonyltris(dimethylphenylarsine)chromium (358 mg.; 41%) as bright yellow prisms, m. p. 98—100°.

(c) *Using triphenylphosphine.* A mixture of triphenylphosphine (3·02 g.) and tricarbonyltoluenechromium (467 mg.) was slowly warmed to 160° and maintained for 2 hr. The resulting deep-red solution was cooled and volatile components were taken off into a trap (acetone–carbon dioxide) at 12 mm. This distillate contained toluene (95·3 mg.; 52%) (estimated from the ultraviolet absorption spectrum in ethanol). The residue was recrystallised twice from chloroform to yield a *p*-complex (971 mg.), m. p. 175—176·8°. This, and the arsenic compound mentioned above, will be discussed in a later communication.

(d) *Using Pyridine.* Tricarbonyltetralinchromium (131 mg.) in pyridine (1 c.c.) was heated under reflux for 1 hr., the red solution was cooled and diluted with ether, and the brown pyridine complex was filtered off. The neutral product was isolated with ether, the solvent was removed through a Fenske column, and the residue was co-distilled with ethanol at 0·02 mm. into a cold trap. Ultraviolet estimation showed the presence of tetralin (27·3 mg.; 42%) in the distillate.

Tricarbonylmesitylenemolybdenum.—A solution of molybdenum hexacarbonyl (1·81 g.) and mesitylene (10 c.c.) in decalin (10 c.c.) was heated under reflux for 3 hr. On cooling, pale yellow needles (1·40 g.; 70%) were deposited and removed by filtration. Recrystallisation from di*iso*propyl ether yielded the complex which decomposed above 150°.

This work was carried out during the tenure by one of us of a research fellowship awarded by the Ethyl Corporation, U.S.A. We also thank the Corporation for generous supplies of chromium hexacarbonyl.

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XUM

114. *Hydrogenation of 4′-Hydroxydiphenylylacetic Acid.*

By W. H. Linnell and H. J. Smith.

A possible synthesis of certain analogues of steroidal hormones required 4-4′-hydroxy*cyclo*hexyl*cyclo*hexylacetic acid. This was obtained by hydrogenation of 4′-hydroxy-4-diphenylylacetic acid.

Kindler (Willgerodt) reaction of 4′-methoxy-4-diphenylyl methyl ketone gave 4′-methoxy-4-diphenylylacetic acid. This was demethylated and the dipotassium salt of the phenolic acid obtained was hydrogenated in aqueous solution at high temperature and pressure, Raney nickel being used as catalyst. The mixture of acids obtained was esterified and separated into phenolic and non-phenolic fractions. The non-phenolic fraction was a mixture of perhydro-compounds and yielded two stereoisomers of 4-4′-hydroxy*cyclo*hexyl-*cyclo*hexylacetic acid (m. p.s 214° and 215·5—216°). These isomers were assigned a *trans*-configuration in the *cyclo*hexylacetic acid ring since each upon oxidation gave the same keto-acid which by Clemmensen reduction gave the known [1] *trans*-4-*cyclo*hexyl*cyclo*-hexylacetic acid.

Hydrogenation of 4′-hydroxy-4-diphenylylacetic acid with shorter time and reduced pressure of hydrogen and Raney nickel : substrate ratio led to the recovery of partially hydrogenated material. The non-phenolic fraction yielded a stereoisomer of 4-4′-hydroxy-*cyclo*hexylphenylacetic acid (m. p. 219—220°). The mother liquors from the acidified mixture, after removal of reduced material and catalyst, slowly gave the other stereoisomer of this acid (m. p. 174·5—175°).

The isolation of *p*-4′-hydroxy*cyclo*hexylphenylacetic acid on partial hydrogenation of 4′-hydroxy-4-diphenylylacetic acid agrees with the findings of other workers [2] where preferential reduction of the phenolic ring in a 4-hydroxydiphenyl system occurs when Raney nickel is used as catalyst under basic conditions.

Experimental

4′-Methoxy-4-diphenylylacetic Acid.—4′-Methoxy-4-diphenylyl methyl ketone (52 g.), morpholine (36 ml.), and sulphur (9·2 g.) were refluxed with stirring for 10 hr. and then poured into sodium hydroxide solution (13%; 750 ml.). The mixture was stirred and refluxed for 12 hr., and then cooled and filtered. The residue was extracted with portions of boiling water and the combined filtrates were acidified. The precipitate was filtered off (crude yield 63%) and recrystallised (from benzene and then aqueous alcohol), giving white plates of *4′-methoxy-4-diphenylylacetic acid*, m. p. 188—188·5° (Found: C, 74·4; H, 6·0; MeO, 12·8%; equiv., 239. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8; MeO, 12·8%; equiv., 242). The p-*bromophenacyl ester* was obtained as white micro-needles (from benzene), m. p. 180° (Found: C, 62·9; H, 4·5; Br, 18·0. $C_{24}H_{21}O_4Br$ requires C, 62·9; H, 4·4; Br, 18·2%). The *amide* formed white micro-needles (from ethanol), m. p. 258—259° (Found: C, 74·3; H, 6·1; N, 5·6. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3; N, 5·8%).

4′-Hydroxy-4-diphenylylacetic Acid.—4-Methoxy-4′-diphenylylacetic acid (30 g.) was refluxed with acetic acid (400 ml.) and hydrobromic acid (48%; 50 ml.) for 16 hr. The acetic acid was then removed and the residue diluted with water to give a crystalline mass (27·2 g.; 96%). Recrystallisation (from acetic acid) gave plates of *4′-hydroxy-4-diphenylylacetic acid*, m. p. 244—245° (Found: C, 73·9; H, 5·4. $C_{14}H_{12}O_3$ requires C, 73·7; H, 5·3%). The *acetate* was obtained (from aqueous alcohol) as white micro-crystals, m. p. 187·5—188·5° (Found: C, 71·2; H, 5·4; Ac, 16·3%; equiv., 269. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2; Ac, 15·9%; equiv., 270).

Perhydrogenation of 4′-Hydroxy-4-diphenylylacetic Acid.—4′-Hydroxy-4-diphenylylacetic acid (10 g.), in water (400 ml.) containing potassium hydroxide (4·92 g.) and W5 Raney nickel (12 g.), was hydrogenated at 240° and 200 atm. for 20 hr. The catalyst was then removed and the filtrate acidified. The precipitate (9·01 g.) was refluxed with methanol (100 ml.) and sulphuric acid (2 ml.) for 9 hr., and the solution then diluted with water and extracted with ether.

[1] Fieser *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 3186.
[2] Dauben and Tanabe, *ibid.*, 1953, **75**, 4969.

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The ethereal extract was washed with sodium hydrogen carbonate solution (5%) and then with potassium hydroxide solution (10%; 3 × 30 ml.). The aqueous layer remaining was refluxed for 7½ hr., filtered, and acidified to give phenolic material (0·06 g.). The ethereal liquors were evaporated and refluxed for 10 hr. with alcoholic potassium hydroxide (10%), and then diluted with water and acidified to give acidic material (7·8 g.; m. p. 163—173°). This material did not absorb at 265 mμ. (*a*) The acidic material (1 g.) was twice recrystallised (from acetic acid) to give material (0·06 g.), m. p. 207·5—209°; two more crystallisations yielded white micro-crystals of 4-4′-*hydroxy*cyclo*hexyl*cyclo*hexylacetic acid*, m. p. 214° (Found: C, 70·8; H, 10·2. $C_{14}H_{24}O_3$ requires C, 70·0; H, 10·1%). The *acetate* was obtained [from light petroleum (b. p. 60—80°)] as white micro-needles, m. p. 96·5—98° (Found: C, 68·6; H, 9·3. $C_{16}H_{26}O_4$ requires C, 68·1; H, 9·3%). (*b*) The acidic material (3 g.) was dissolved in N-sodium hydroxide solution (20 ml.) and water (80 ml.). The solution was filtered and sodium nitrate (10 g.) dissolved in it by boiling, and the solution then set aside at room temperature for some hours. The acid was recovered from the precipitated sodium salt (1·074 g.; m. p. 189—200°). This procedure was then repeated with half the quantities of reagents given above. The recovered material, (0·55 g.; m. p. 200—206°) was twice recrystallised (from aqueous acetic acid), giving white micro-crystals of 4-4′-*hydroxy*cyclo*hexyl*cyclo*hexylacetic acid*, m. p. 215·5—216°, which depressed the melting point of the isomeric acid described above (*a*) (Found: C, 69·9; H, 10·2%; equiv., 244. $C_{14}H_{24}O_3$ requires C, 70·0; H, 10·1%; equiv., 240). The *acetate* was obtained [from light petroleum (b. p. 60—80°)] as white micro-crystals, m. p. 140—141·5° (Found: C, 68·3; H, 9·4. $C_{16}H_{26}O_4$ requires C, 68·1; H, 9·3%), which depressed the melting point of the isomeric acetate described above (*a*).

Oxidation of 4-4′-*Hydroxy*cyclo*hexyl*cyclo*hexylacetic Acid.*—The stereoisomer (0·25 g.), m. p. 214°, of 4-4′-hydroxy*cyclo*hexyl*cyclo*hexylacetic acid was dissolved in acetic acid and oxidised with chromium trioxide in aqueous acetic acid. The solution was worked up in the usual manner to give a glass (0·17 g.). The ketonic fraction was separated by preparation of the semicarbazone which upon subsequent hydrolysis and recrystallisation (from carbon tetrachloride) gave micro-needles of 4-4′-*oxo*cyclo*hexyl*cyclo*hexylacetic acid*, m. p. 138·5° (Found: C, 70·3; H, 9·2%; equiv., 243. $C_{14}H_{22}O_3$ requires C, 70·5; H, 9·3%; equiv., 238). The *semicarbazone* (from aqueous acetic acid) had m. p. 205·5—206·5° (decomp.) (Found: C, 60·4; H, 8·2; N, 13·7. $C_{15}H_{25}O_3N_3$ requires C, 61·0; H, 8·5; N, 14·2%). The *ethyl ester* 2 : 4-*dinitrophenylhydrazone* was obtained (from ethanol) as long, orange needles, m. p. 141° (Found: C, 59·2; H, 6·9; N, 12·5. $C_{22}H_{30}O_6N_4$ requires C, 59·2; H, 6·8; N, 12·6%).

The stereoisomer, m. p. 215·5—216°, of 4-4′-hydroxy*cyclo*hexyl*cyclo*hexylacetic acid was similarly oxidised to give material, m. p. and mixed m. p. 138·5° with the aforementioned sample of 4-4′-oxo*cyclo*hexyl*cyclo*hexylacetic acid. The ethyl ester 2 : 4-dinitrophenylhydrazone was obtained as long orange needles, m. p. and mixed m. p. 141° with the corresponding derivative of the aforementioned sample of 4-4′-oxo*cyclo*hexyl*cyclo*hexylacetic acid.

Clemmensen Reduction of 4-4′-*Oxo*cyclo*hexyl*cyclo*hexylacetic Acid.*—4-4′-Oxo*cyclo*hexyl*cyclo*hexylacetic acid (0·45 g.) was refluxed with amalgamated zinc (10 g.), water (20 ml.) concentrated hydrochloric acid (25 ml.), and acetic acid (25 ml.) for 11½ hr. The supernatant liquid was decanted off and cooled to give a flocculent precipitate (0·35 g.; m. p. 131—132°). Recrystallisation (from aqueous acetic acid) gave white micro-crystals of *trans*-4-*cyclo*hexyl*cyclo*hexylacetic acid, m. p. and mixed m. p. 136—137° with an authentic sample (Found: C, 75·2; H, 10·5%; equiv., 224. Calc. for $C_{14}H_{24}O_2$: C, 75·0; H, 10·8%; equiv., 224). The p-*bromophenacyl ester* was obtained (from aqueous ethanol) as felted micro-needles, m. p. 142·5—143·5° (Found: C, 62·2; H, 7·0; Br, 18·6. $C_{22}H_{29}O_3Br$ requires C, 62·7; H, 6·9; Br, 19·0%).

Partial Hydrogenation of 4′-*Hydroxy*-4-*diphenylylacetic Acid.*—4′-Hydroxy-4-diphenylylacetic acid (5 g.), in water (400 ml.) containing potassium hydroxide (2·46 g.) and W5 Raney nickel (3 g.), was hydrogenated at 240° and 170 atm. for 10 hr. The suspension was then filtered and acidified to give a mixture of acids (3·75 g.; m. p. 179—190°). This material was separated into phenolic and non-phenolic fractions as previously described. The phenolic fraction gave a white solid (0·51 g.; m. p. 235—239°) which on crystallisation (from aqueous acetic acid) gave plates, m. p. and mixed m. p. 244° with authentic 4′-hydroxy-4-diphenylylacetic acid. The non-phenolic fraction gave a mixture of acids (1·79 g.; m. p. 199—203°) which upon repeated crystallisation (from aqueous acetic acid) gave micro-needles of p-4′-*hydroxy*cyclo*hexylphenylacetic acid*, m. p. 219—220° (Found: C, 71·2; H, 7·7. $C_{14}H_{18}O_3$

requires C, 71·8; H, 7·7%); $\lambda_{max.}$ (in 95% ethanol) 263 mμ (log ε 2·60) [cf.[3] toluene, $\lambda_{max.}$ 262 (log ε 2·45); *p-cyclo*hexylphenol, $\lambda_{max.}$ 278 (log ε 3·35)]. The *acetate* was obtained as white micro-needles [from light petroleum (b. p. 60—80°)], m. p. 115·5° (Found: C, 69·7; H, 7·3. $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·3%).

After removal of nickel and precipitated acids from the reaction solution, the mother liquors slowly deposited (3 days) an amorphous solid (0·24 g.; m. p. 166—168°). Repeated crystallisation (from aqueous acetic acid) gave white micro-crystals of p-4′-*hydroxy*cyclo*hexylacetic acid*, m. p. 174·5—175° depressed on admixture with the stereoisomer, m. p. 219—220° (Found: C, 71·5; H, 7·9. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). The *acetate* was obtained [from light petroleum (b. p. 60—80°)] as long white needles, m. p. 121° (depressed on admixture with the acetate of the stereoisomer, m. p. 219—220°); $\lambda_{max.}$ (95% ethanol) 262·5 (log ε 2·54) (Found: C, 70·0; H, 7·2. $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·3%).

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School of Pharmacy, University of London. [*Received, September 30th*, 1958.]

[3] Friedel and Orchin, "Ultra-violet Spectra of Aromatic Compounds," John Wiley and Sons, New York, 1951.

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115. *The Reaction of* 1 : 4-*Dichloro*-2 : 3-*epoxybutane with Sodium Methoxide.*

By A. W. Adams, E. G. E. Hawkins, G. F. Oldham, and R. D. Thompson.

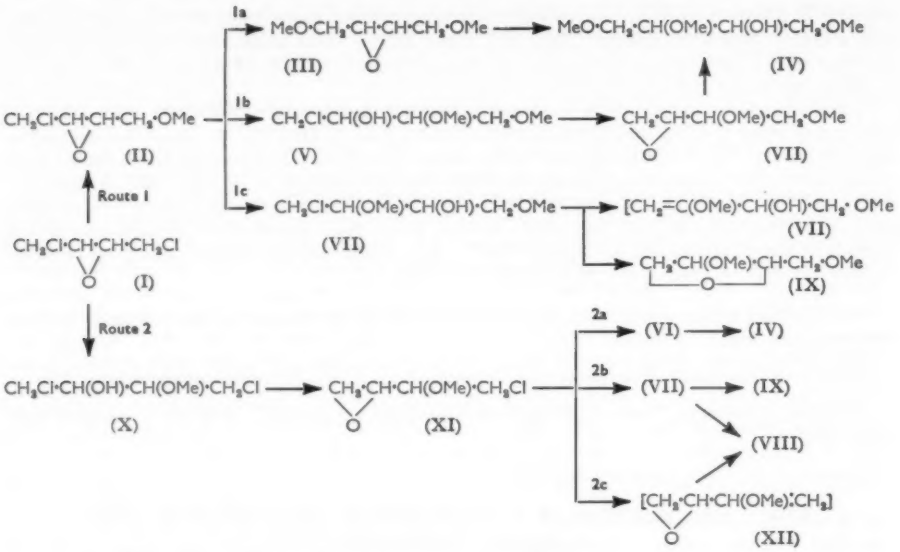
The reaction of 1 : 4-dichloro-2 : 3-epoxybutane with sodium methoxide has been shown to provide a complex mixture, including 1 : 3 : 4-trimethoxybutan-2-ol, 3-methoxy-2-methoxymethyloxetan, and *cis*- and *trans*-4-chloro-1-methoxybut-3-en-2-ol. Possible reaction routes are considered.

The reaction of simple epoxides with alkali (or metal alkoxides) normally leads to glycols (or glycol monoethers);[1] epichlorohydrin similarly yields glycerol (or glycerol ethers).[2] A dichloroepoxyalkane, 1 : 2-dichloro-3 : 4-epoxybutane, has been found to provide under alkaline conditions mainly 2-chloro-3 : 4-epoxybut-1-ene by preferential loss of hydrogen chloride, although further reaction with a metal alkoxide brings about opening of the epoxide ring.[3] Studies on the points of initial attack of 1-bromo-2 : 3- and 3-bromo-1 : 2-epoxybutane by sodium methoxide [4] and sodium phenoxide [5] have indicated that variations in the reactant cause some alteration in the mode of attack, so that sometimes the halogen is first replaced and at other times the epoxide ring is first opened. However, a metal alkoxide and the symmetrical 1 : 4-dichloro-2 : 3-epoxybutane could lead to a variety of products, depending on the relative reactivities of the chloro-atoms and the epoxy-group in this molecule. Possible reaction routes (using sodium methoxide) are shown in the diagram.

Route 1 involves initial replacement of chlorine by methoxyl followed either by similar replacement of the second chlorine atom (1a) or by opening of the epoxide ring in one of two directions (1b or 1c). Both routes (1a) and (1b) would lead finally to 1 : 3 : 4-trimethoxybutan-2-ol (IV), whereas route (1c) might be expected to yield either 1 : 3-dimethoxybut-3-en-2-ol (VIII) or 3-methoxy-2-methoxymethyloxetan (IX). Route 2, on the other hand, involves opening of the epoxide ring followed by immediate ring closure to 1-chloro-3 : 4-epoxy-2-methoxybutane (XI) and thence by three possible routes to

[1] Graham, Millidge, and Young, *J.*, 1954, 2180; Swern, Billen, and Knight, *J. Amer. Chem. Soc.*, 1949, **71**, 1152; Kadesch, *ibid.*, 1946, **68**, 41.
[2] Huntress, "Organic Chlorine Compounds," John Wiley & Sons, New York, 1948, pp. 668—669.
[3] Hawkins, *J.*, 1959, 248.
[4] Waters and VanderWerf, *J. Amer. Chem. Soc.*, 1954, **76**, 709.
[5] Rowton and Russell, *J. Org. Chem.*, 1958, **23**, 1002.

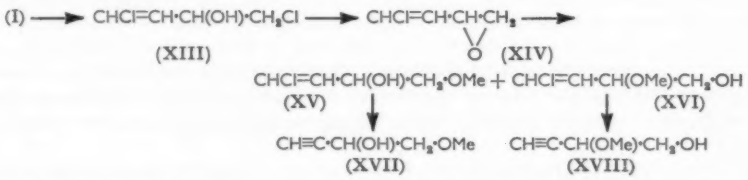
XUM



1 : 3 : 4-trimethoxybutan-2-ol (route 2a), to the oxetan (IX) or unsaturated hydroxy-ether (VIII) (routes 2b, 2c).

Treatment of the dichloroepoxybutane with an excess of sodium methoxide in boiling methanol led to a product with a wide boiling range. Examination of the distillation fractions showed that two of the predicted compounds, *i.e.*, trimethoxybutanol and the oxetan, were major constituents (*ca.* 40% and 16% respectively), but the dimethoxybutenol (VIII) could not be identified.

However, there were other, unexpected, components in the product: the bulk of these was *trans*-4-chloro-1-methoxybut-3-en-2-ol (XV) (*ca.* 19%), with smaller amounts of the corresponding *cis*-isomer and *trans*-4-chloro-2-methoxybut-3-en-1-ol (XVI), and also 1-methoxybut-3-yn-2-ol (XVII) (up to 6%). These compounds presumably arose by a third route, as follows:

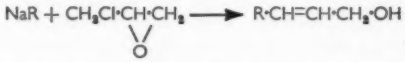


The products from this third route were isolated by gas-phase chromatography on a Tween–Celite column at 160°. Infrared spectroscopy showed the presence of hydroxyl and methoxyl in each compound; the relative positions of these groups were found by catalytic hydrogenation (using an alkaline Raney nickel catalyst) to 1-methoxybutan-2-ol (from XV and XVII) or 2-methoxybutan-1-ol (from XVI). The presence of the *trans*-isomers of (XV) and (XVI) was demonstrated by the appearance of a strong band at 938 cm.$^{-1}$ (*trans*-1-halogen-substituted alk-1-ene [6]) in their infrared spectra: the spectra of the corresponding *cis*-isomers were similar in many ways except that the 938 cm.$^{-1}$ band was absent. A band at 3300 cm.$^{-1}$ in the spectrum of (XVII) agreed with the postulated acetylenic

[6] Bellamy, "The Infra Red Spectra of Complex Molecules," Methuen, London, 1958, p. 46.

structure.[7] The epoxide (XIV), not identified amongst the reaction products, was synthesised from 1-chlorobutadiene *via* the bromohydrin. From its spectrum this synthetic epoxide appeared to be largely the *trans*-compound, but reaction with acid methanol yielded *ca.* 70% of *cis*-4-chloro-2-methoxybut-3-en-1-ol (XVI) with *ca.* 30% of the *trans*-isomer, whilst with sodium methoxide it provided a mixture of the two acetylenic compounds (XVII and XVIII), together with *cis*- and *trans*-compounds (XV) and (XVI) [mainly the *cis*- and *trans*-components (XV)]. The products from the synthetic 1-chloro-3 : 4-epoxybut-1-ene and from 1 : 4-dichloro-2 : 3-epoxybutane were compared by means of their physical properties and by mixed m.p.s of their 3 : 5-dinitrobenzoates.

Isomerisation of epoxides to unsaturated alcohols in the presence of acid is known,[8] but there are few references to this rearrangement under alkaline conditions; however, the products of reaction of epichlorohydrin with sodium toluene-*p*-sulphinate,[9] sodium cyanide,[10] and sodium acetylide [11] suggest that a similar mechanism was involved in these cases.



The acetylenic secondary alcohol (XVII) evidently arose by dehydrochlorination of the compound (XV). A similar (slow) production of methoxybutynols has been noticed on reaction of 3-chloro-1-methoxybut-3-en-2-ol or 3-chloro-2-methoxybut-3-en-1-ol with sodium methoxide.[12]

Other compounds identified in minor amounts in the product included diacetyl, 1-chloro-2 : 3-epoxy-4-methoxybutane (II), and 1 : 2-epoxy-3 : 4-dimethoxybutane (VI).

In order to obtain further information on the intermediate stages of this reaction, 1 : 4-dichloro-2 : 3-epoxybutane was treated with only one mol. of sodium methoxide. The product contained, in addition to much starting material and the compounds obtained when an excess of sodium methoxide was used, a large amount of 4-chloro-1 : 3-dimethoxybutan-2-ol (VII), with some 1-chloro-3 : 4-dimethoxybutan-2-ol (V), 2 : 3-epoxy-1 : 4-dimethoxybutane (III), and possibly a trace of 1-chloro-3 : 4-epoxy-2-methoxybutane (XI).

From the above it is evident that all three routes are involved in the reaction, although the relatively large amount of trimethoxybutanol isolated suggested that route 1 is the preferred one. That the trimethoxybutanol arises mainly by this route was demonstrated by study of the reaction of the intermediate epoxide (II) with sodium methoxide: there were produced trimethoxybutanol (IV; *ca.* 80%), the oxetan (IX; *ca.* 8%), 2 : 3-epoxy-1 : 4-dimethoxybutane (III; 2%), and unchanged epoxide (II; 6%). The small amount of oxetan obtained from (II) evidently arose by route (1c) since 4-chloro-1 : 3-dimethoxybutan-2-ol (VII) under similar conditions gave this compound (IX) almost completely, with less than 10% of the ether (IV). The majority of the oxetan formed in the overall reaction arose *via* route 2; both of the intermediates (X) and (XI) independently gave 75—80% of (IX) and 20—25% of (IV) on treatment with sodium methoxide.

It appears, therefore, that the reaction of 1 : 4-dichloro-2 : 3-epoxybutane with sodium methoxide follows largely the routes (1a), (1b), (2b), and (3) and only slightly routes (1c) and (2b); there is no evidence that route (2c) is involved.

Most of the compounds formulated in the diagram were synthesised as reference materials for spectroscopy and chromatography, starting from 1 : 4-dichloro-2 : 3-epoxybutane and 1 : 2-dichloro-3 : 4-epoxybutane. In these syntheses the direction of ring opening of several epoxides was found to differ from that generally accepted. 1 : 2-Epoxides normally provide secondary alcohols under alkaline, and primary alcohols under

[7] Ref. 6, p. 58.
[8] Hickinbottom, *J.*, 1948, 1331; Gasson, Graham, Millidge, Robson, Webster, Wild, and Young, *J.*, 1954, 2170.
[9] Culvenor, Davies, and Savige, *J.*, 1949, 2198.
[10] Culvenor, Davies, and Haley, *J.*, 1950, 3123.
[11] Haynes, Heilbron, Jones, and Sondheimer, *J.*, 1947, 1583.
[12] Hawkins, unpublished work.

acid, reaction conditions;[1] however, epichlorohydrin gives mainly secondary alcohols under both sets of conditions (Swern *et al.*[2]), and it seems probable that the way the ring opens depends to some extent on the substituents in the epoxide molecule and on the structure of the reacting alcohol (Swern *et al.*[2]).

1 : 2-Dichloro-3 : 4-epoxybutane with acid methanol gave the secondary alcohol, 3 : 4-dichloro-1-methoxybutan-2-ol; this was proved by conversion of the product into 1-chloro-2 : 3-epoxy-4-methoxybutane by alkali. Similarly, 1 : 2-epoxy-3 : 4-dimethoxybutane (VI) with acid methanol yielded the same 1 : 3 : 4-trimethoxybutan-2-ol as did 2 : 3-epoxy-1 : 4-dimethoxybutane (III); and with hydrogen chloride the epoxide (VI) gave 1-chloro-3 : 4-dimethoxybutan-2-ol (V), one of the products of reaction of 1-chloro-2 : 3-epoxy-4-methoxybutane (II) with acid methanol. 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) with hydrogen chloride also gave a secondary alcohol, 1 : 4-dichloro-3-methoxybutan-2-ol (X), identical with that obtained by addition of acid methanol to 1 : 4-dichloro-2 : 3-epoxybutane (I). 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) with acid methanol forms the secondary alcohol, 4-chloro-1 : 3-dimethoxybutan-2-ol (VII); this alcohol, and the original epoxide (XI), react with sodium methoxide to give 2-methoxymethyl-3-methoxyoxetan (IX), demonstrating that both acid and alkaline methanol here open the epoxide ring in the same direction.

However, 2-chloro-3 : 4-epoxybut-1-ene follows the normal pattern, providing the corresponding secondary alcohol with sodium methoxide and the primary alcohol with acid methanol. The reactions of 1-chloro-3 : 4-epoxybut-1-ene with acid methanol and sodium methoxide have already been mentioned.

The 1 : 4-dichloro-2 : 3-epoxybutane used in this work was prepared by oxidation of 1 : 4-dichlorobut-2-ene with performic acid, with use of a shorter reaction time and a smaller quantity of formic acid ($\frac{1}{4}$—$\frac{1}{2}$ mol.) than was used by Owen.[13] Owen reported that he isolated only *meso*-1 : 4-dichlorobutane-2 : 3-diol, m. p. 127°, from this reaction; in our work, however, with a mixture of *cis*- and *trans*-dichlorobutene, both the *meso*- and the (±)-glycol were isolated by fractional crystallisation of the products of hydration of the epoxide. The mixture of *cis*- and *trans*-epoxide was not appreciably separable by distillation.

Experimental

Preparation of 1 : 4-*Dichloro*-2 : 3-*epoxybutane*.—(a) *Using performic acid*. 85% Hydrogen peroxide (32 c.c.) was added, with stirring, during 1 hr. to a mixture of 1 : 4-dichlorobut-2-ene (mixture of *trans* 70% and *cis* 30%; 125 g.) and 98—100% formic acid (23 c.c.) at 60°; stirring at 60° was maintained for a further 2 hr. The product was cooled, added to water (*ca.* 400 c.c.), and extracted with ether. The aqueous phase gave no residue on evaporation, and the ethereal phase on drying, evaporation, and distillation gave fractions: (1) (4·7 g.), b. p. $<150°$; (2) (49·2 g.), b. p. 150—160°, n_D^{20} 1·4870; (3) (11·8 g.), b. p. 160—180°, n_D^{20} 1·4847; (4) (52·6 g.), b. p. 180—186·5°, n_D^{20} 1·4771; and residue (3·8 g.). Fraction 2 was unchanged dichlorobutene, and fraction 4 was the epoxide.

Redistillation gave the pure *epoxide*, b. p. 187—188°, n_D^{20} 1·4763 (Found: C, 34·15; H, 4·3; Cl, 50·1. $C_4H_6OCl_2$ requires C, 34·0; H, 4·25; Cl, 50·4%). The Nicholet–Poulter and other methods for epoxide determination gave unsatisfactory figures with this compound.

(b) Via *the bromohydrin*. *N*-Bromosuccinimide (19 g.) in water (80 c.c.) was stirred at room temperature with 1 : 4-dichlorobut-2-ene (12·5 g.) in ether (80 c.c.) until all the solid had disappeared (21½ hr.). The combined ethereal layer and extracts were washed, dried, and distilled to give the *bromohydrin* (16·3 g.), b. p. 70—80°/0·7 mm., n_D^{20} 1·5352 (Found: C, 21·8; H, 3·4; Br, 36·0; Cl, 31·7. $C_4H_5OBrCl_2$ requires C, 21·8; H, 2·2; Br, 36·3; Cl, 32·3%).

A solution of sodium hydroxide (4·2 g.) in water (15 c.c.) was added, during 10 min. at room temperature, to a stirred mixture of the bromohydrin (22 g.) and water (10 c.c.); after stirring had been continued for 1½ hr. the product was worked up to give the epoxide (6·8 g.), b. p. 181—190°, n_D^{20} 1·4810 (Found: Cl, 50·9%), identical spectroscopically with that obtained by oxidation by performic acid.

[13] Owen, *J.*, 1949, 241.

Hydration of 1 : 4-*Dichloro*-2 : 3-*epoxybutane.*—The epoxide (400 g.) was added gradually to 98—100% formic acid (200 g.); stirring was necessary to prevent local overheating in this exothermic reaction. The mixture was then heated under reflux for a short time, water was added, and boiling continued. Most of the formic acid was removed in steam, and the residual acid and water were evaporated under reduced pressure to leave the semi-solid, crude glycol. Crystallisation from carbon tetrachloride–ethyl acetate gave the *meso*-1 : 4-dichlorobutane-2 : 3-diol (224·6 g.; m. p. 124—126°); recrystallisation from ethyl acetate raised the m. p. to 126—129° (cf. ref. 13) (Found: C, 30·2; H, 5·0; Cl, 44·5. Calc. for $C_4H_8O_2Cl_2$: C, 30·2; H, 5·0; Cl, 44·7%). The diol provided a *bisphenylurethane*, m. p. 222—224° (from acetone) (Found: C, 54·6; H, 4·7; Cl, 17·7; N, 7·1. $C_{18}H_{18}O_4N_2Cl_2$ requires C, 54·4; H, 4·5; Cl, 17·9; N, 7·05%), almost insoluble in benzene.

The mother-liquors were distilled and appropriate cuts crystallised and recrystallised, to give the (±)-glycol (83·0 g.), m. p. 58—60° (Found: C, 30·4; H, 5·1; Cl, 44·5%) [*bisphenylurethane*, m. p. 170—172° (from benzene) (Found: C, 54·6; H, 4·4; Cl, 17·5; N, 7·0%)].

Reaction of 1 : 4-*Dichloro*-2 : 3-*epoxybutane with Sodium Methoxide.*—The products obtained from this reaction were identified by comparison with the synthetic compounds described below by infrared spectra, gas-phase chromatography, m. p. of derivatives, and catalytic hydrogenation. The chromatographic separations were carried out on columns of Tween–Celite at 160° or Apiezon–Celite at 117° with nitrogen carrier gas and a hydrogen-flame detector; Tween 60 is polyoxyethylene sorbitan monostearate, the Apiezon K was a high-vacuum grease from Messrs. Edwards, and the Celite was of 100—120 mesh.

(a) *Using 2·5 mols. of sodium methoxide.* (i) The epoxide (176 g.), in methanol (20 c.c.), was heated under reflux with sodium (75·2 g.) in methanol (600 c.c.) for 4 hr.; little change in the sodium methoxide content occurred during the last 2 hr., and *ca.* 80% of the calculated amount

Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}	Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}
1	58—61°	20·9	1·4256	12	85—88°	3·7	1·4618
2	61—63	5·3	1·4272	13	88—92	4·2	1·4538
3	63—65	5·1	1·4295	14	92—95	4·9	1·4430
4	65—70	4·8	1·4329	15	95—96	6·8	1·4362
5	70—71	6·3	1·4382	16	96—96·5	37·4	1·4319
6	71—75	4·8	1·4471	17	96·5—98	7·3	1·4339
7	75—80	5·0	1·4558	18	98—106	4·5	1·4390
8	80—82	6·4	1·4620	19	106—130	1·7	1·4461
9	82—83	8·4	1·4645	20	130—140	1·2	1·4549
10	83—84	10·1	1·4655	Res.	—	15·1	—
11	84—85	2·7	1·4647				

(based on chlorine) had then been consumed. The excess of alkali was exactly neutralised with ethereal hydrogen chloride, the product filtered, and the filtrate evaporated and distilled (4 ft., helices-packed column) to give fractions as tabulated.

Infrared spectroscopy showed that the first five fractions consisted largely of 3-methoxy-2-methoxymethyloxetan, but that a carbonyl compound was present in fractions 2—8 (maximum in fr. 6). Fractions 5—17 (maximum in fr. 10) contained an unsaturated compound with a *trans*-1-substituted alk-1-ene system and hydroxyl and methoxyl groups. Above fraction 12 the main constituent appeared to be 1 : 3 : 4-trimethoxybutan-2-ol.

Examination of fractions 4—8 by gas-phase chromatography on a Tween–Celite column at 160° showed that the oxetan content decreased from 55% (fr. 4) to 2% (fr. 7) and that there were also present in fractions 4—7 1-methoxybut-3-yn-2-ol (up to 25% in fr. 5), an unidentified material which yielded diacetyl 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 326—327°, and 1-chloro-2 : 3-epoxy-4-methoxybutane. Fractions 6—8 contained increasing quantities of mixed 4-chloromethoxybut-3-enols (fraction 7 contained 80%, and fraction 8·88%); the *cis*-isomers were separable from the *trans*-isomers on the column used but the secondary alcohols were not separable from the corresponding primary alcohols, and the ratio of these was obtained by catalytic hydrogenation on alkaline Raney nickel. Thus fraction 7 contained 40% of *cis*-isomers (4 parts secondary alcohol : 1 part primary alcohol) and 40% of *trans*-isomers (4·7 parts secondary alcohol : 1 part primary alcohol). The *cis*-isomer, separated chromatographically, provided the 3 : 5-*dinitrobenzoate*, m. p. 68·5—70·5° (Found: Cl, 10·3. $C_{12}H_{11}O_7N_2Cl$ requires Cl, 10·7%), of *cis*-4-chloro-1-methoxybut-3-en-2-ol and the *trans*-isomer similarly gave the 3 : 5-*dinitrobenzoate*, m. p. 75—77° (Found: C, 43·2; H, 3·3; Cl, 10·75; N, 8·4. $C_{12}H_{11}O_7N_2Cl$ requires C, 43·6; H, 3·3; Cl, 10·7; N, 8·5%).

Fraction 10 provided two 3 : 5-dinitrobenzoates. The first, m. p. 75—77°, was identical with that above (*trans*-4-chloro-1-methoxybut-3-en-2-yl), and the second, obtained by fractional crystallisation of the mother-liquors (m. p. 96—98°) (Found: C, 43·3; H, 3·3; Cl, 11·1; N, 8·5%), was trans-4-*chloro*-2-*methoxybut*-3-*enyl* 3 : 5-*dinitrobenzoate*. This fraction also provided an α-*naphthylurethane*, m. p. 78—80° (Found: C, 62·6; H, 5·1; Cl, 11·9; N, 4·6. $C_{16}H_{16}O_3NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%), probably of the secondary alcohol. Catalytic hydrogenation of this fraction gave mainly 1-methoxybutan-2-ol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 89—91°) with a small amount of 2-methoxybutan-1-ol (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 60—62°).

Fraction 12 was found to be entirely *trans*-4-chloromethoxybut-3-enols by chromatography (4·4 parts of secondary alcohol : 1 part of primary alcohol, by hydrogenation) and provided the same two 3 : 5-dinitrobenzoates as fraction 10.

Fraction 16 yielded the 3 : 5-*dinitrobenzoate*, m. p. and mixed m. p. 90—91° (Found: C, 47·3; H, 5·45; N, 7·9. $C_{14}H_{18}O_9N_2$ requires C, 46·9; H, 5·0; Cl, 7·8%), of 1 : 3 : 4-trimethoxybutan-2-ol.

(ii) The reaction (i) was carried out on a one-tenth scale; after removal of the solvent the total product was flash-distilled and analysed chromatographically, on both a Tween–Celite column at 160° and an Apiezon–Celite column at 117°. The following approximate analysis was obtained: 3-methoxy-2-methoxymethyloxetan (16%), 1-methoxybut-3-yn-2-ol (6%), 1 : 2-epoxy-3 : 4-dimethoxybutane (1—2%), 1-chloro-2 : 3-epoxy-4-methoxybutane (1·5%), a mixture (3%) of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol, a mixture (24%) of *trans*-4-chloro-1-methoxybut-3-en-2-ol (80%) and *trans*-4-chloro-2-methoxybut-3-en-1-ol (20%), 1 : 3 : 4-trimethoxybutan-2-ol (40%), and an unknown compound (7—8%).

(b) *Using* 1 *mol. of sodium methoxide.* (i) 1 : 4-Dichloro-2 : 3-epoxybutane (176 g.) in methanol (20 c.c.) was heated under reflux with a solution of sodium (30 g.) in methanol (300 c.c.) for *ca.* 4½ hr.; nearly all the sodium methoxide reacted. Working up as before finally gave the fractions tabulated.

Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}	Fr.	B. p. (13 mm.)	Wt. (g.)	n_D^{20}
1	60—63°	6·1	1·4281	11	78—80°	7·1	1·4649
2	63—65	2·7	1·4306	12	80—86	5·3	1·4625
3	65—67	4·3	1·4344	13	86—90	1·9	1·4586
4	67—70	4·6	1·4382	14	90—97	4·9	1·4502
5	70—72	7·3	1·4477	15	97—99	3·3	1·4447
6	72—74	8·6	1·4536	16	99—101	5·7	1·4429
7	74—75	20·5	1·4591	17	101—104	19·3	1·4438
8	75—76	14·3	1·4632	18	104—106	13·1	1·4519
9	76	18·7	1·4658	Res.	—	2·7	—
10	76—78	20·7	1·4653				

Infrared spectroscopic examination showed that fractions 1 and 2 were largely the oxetan, which was present up to fraction 5. Fractions 5—12 contained 1-chloro-2 : 3-epoxy-4-methoxybutane and some unchanged dichloroepoxide. The *trans*-unsaturated chloro-compound (938 cm.$^{-1}$ band) appeared in fractions 10—16, and the later fractions were mainly 1 : 3 : 4-trimethoxybutan-2-ol although fractions 15 and 16 probably contained chlorodimethoxybutanols.

Fraction 16 gave the 3 : 5-dinitrobenzoate of 1 : 3 : 4-trimethoxybutan-2-ol, and fraction 18 provided the 3 : 5-*dinitrobenzoate*, m. p. and mixed m. p. 106—108° (Found: C, 43·3; H, 4·5; Cl, 10·0; N, 7·55. $C_{13}H_{15}O_8N_2Cl$ requires C, 43·0; H, 4·1; Cl, 9·8; N, 7·7%), of 4-chloro-1 : 3-dimethoxybutan-2-ol.

(ii) The experiment (i) was repeated on a one-tenth scale, and the solvent-free product flash-distilled and examined chromatographically on Tween–Celite at 160° and Apiezon–Celite at 117°. The following approximate analysis was obtained: 3-methoxy-2-methoxymethyloxetan (11%), 1-methoxybut-3-yn-2-ol (3%), 1 : 2-epoxy-3 : 4-dimethoxybutane (0·4%), a mixture (3%) of 2 : 3-epoxy-1 : 4-dimethoxybutane and 1-chloro-3 : 4-epoxy-2-methoxybutane, 1-chloro-2 : 3-epoxy-4-methoxybutane (14%), unchanged 1 : 4-dichloro-2 : 3-epoxybutane (20%), a mixture (5%) of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol, a mixture (14%) of *trans*-4-chloro-1-methoxybut-3-en-2-ol and *trans*-4-chloro-2-methoxybut-3-en-1-ol, 1 : 3 : 4-trimethoxybutan-2-ol (13%), 4-chloro-1 : 3-dimethoxybutan-2-ol (16%), and an unknown component (<1%).

Preparation of Reference Compounds.—1-*Chloro*-3 : 4-*epoxybut*-1-*ene*. (*a*) Preparation.

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1-Chlorobutadiene (80 g.) in ether (1000 c.c.) was stirred with *N*-bromosuccinimide (150 g.) in water (1 l.) at room temperature until all the solid had dissolved. The ethereal extracts were evaporated, and the crude bromohydrin, without further purification, was stirred with sodium hydroxide (40 g.) in water (80 c.c.) at *ca.* 30° for 1 hr. The ethereal extract of the product, on distillation, provided the *epoxide* (27·6 g.), b. p. 70—72°/100 mm., 126°/1 atm., n_D^{20} 1·4698 (Found: C, 45·4; H, 5·1; Cl, 34·25%; epoxide equiv., 117. C_4H_5OCl requires C, 45·9; H, 4·8; Cl, 34·0%; epoxide equiv., 104·5).

(*b*) Reaction with acid methanol. The epoxide (7·5 g.) was heated under reflux for 2 hr. with methanol (25 c.c.) containing a trace of sulphuric acid. The solution was cooled, neutralised with solid sodium hydrogen carbonate, filtered, diluted with ether, and washed with water. Distillation gave 4-chloromethoxybut-3-enols (4·2 g.), b. p. 82·5—84·5°/15 mm., n_D^{20} 1·4650, and a residue (1·3 g.). A sample on catalytic hydrogenation yielded entirely 2-methoxybutan-1-ol, and chromatography showed that ratio of *cis* : *trans* was *ca.* 7 : 3. Hence the product consisted of *cis*- (70%) and *trans*-4-chloro-2-methoxybut-3-en-1-ol (30%). The *α-naphthylurethane*, m. p. 77—78·5° (Found: C, 62·7; H, 5·2; Cl, 11·85; N, 4·3. $C_{16}H_{16}O_2NCl$ requires C, 62·8; H, 5·2; Cl, 11·6; N, 4·6%), and 3 : 5-*dinitrobenzoate*, m. p. 90·5—92·5° (Found: C, 43·9; H, 3·65; Cl, 11·2; N, 8·3. $C_{12}H_{11}O_7N_2Cl$ requires C, 43·6; H, 3·3; Cl, 10·7; N, 8·5%), were derivatives of *cis*-4-chloro-2-methoxybut-3-en-1-ol.

(*c*) Reaction with sodium methoxide. The epoxide (15·6 g.) was heated under reflux for 6 hr. with sodium methoxide (from 1·5 g. of sodium) in methanol (25 c.c.). After normal working up and distillation there were obtained fractions: (1) (1·7 g.), b. p. 66—70°/14 mm., n_D^{20} 1·4480; (2) (1·4 g.), b. p. 70—72°/14 mm., n_D^{20} 1·4505; (3) (1·7 g.), b. p. 72—75°/14 mm., n_D^{20} 1·4524; (4) (2·7 g.), b. p. 75—80·5°/14 mm., n_D^{20} 1·4600; (5) (3·8 g.), b. p. 80·5—83·5°/14 mm., n_D^{20} 1·4636; and a residue (2·6 g.).

Spectroscopy showed that fractions 1—4 contained acetylenic material in decreasing amounts, and fractions 3—5 contained compounds with a 1-substituted vinyl group (partly *trans*); all fractions contained hydroxyl and methoxyl groups.

A portion of the combined product was chromatographed on a Tween–Celite column at 160° and four fractions were separated: these were examined separately. Fraction (i) consisted of 2-methoxybut-3-yn-1-ol [3 : 5-*dinitrobenzoate*, m. p. 94—95° (Found: C, 48·5; H, 3·5; N, 9·5, 9·6. $C_{12}H_{10}O_7N_2$ requires C, 49·0; H, 3·4; N, 9·5%)], yielding entirely 2-methoxybutan-1-ol on catalytic hydrogenation. Fraction (ii) was 1-methoxybut-3-yn-2-ol [3 : 5-*dinitrobenzoate*, m. p. 54—55·5° (Found: C, 48·9; H, 3·5; N, 9·7, 9·4%)], and gave 1-methoxybutan-2-ol on hydrogenation. Fraction (iii) was a mixture of *cis*-4-chloro-1-methoxybut-3-en-2-ol and *cis*-4-chloro-2-methoxybut-3-en-1-ol (ratio 1·8 : 1 by hydrogenation); it provided the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 90—91·5°, of the primary alcohol, and an impure derivative, m. p. 64—67°, of the secondary alcohol. Fraction (iv) was a mixture of *trans*-4-chloro-1-methoxybut-3-en-2-ol and *trans*-4-chloro-2-methoxybut-3-en-1-ol (ratio 3 : 1 by hydrogenation); only the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 75—76°, of the secondary alcohol was isolated from this fraction.

3 : 4-*Dichloro*-1-*methoxybutan*-2-*ol*. 1 : 2-Dichloro-3 : 4-epoxybutane [3] (150 g.; 70% of low-boiling, 30% of high-boiling isomer) and methanol (250 c.c.) containing sulphuric acid (2 c.c.) were heated under reflux for 24 hr. The excess of methanol was distilled off, and the residue diluted with water and extracted with ether. Distillation gave the *dichloromethoxybutanol* (152·8 g.), b. p. 111—112°/13 mm., n_D^{20} 1·4745 (Found: OMe 18·0. $C_4H_7OCl_2$·OMe requires OMe, 17·9%), chromatographically homogeneous [*phenylurethane*, m. p. 104·5—105·5° (Found: C, 49·3; H, 5·2; Cl, 24·0; N, 4·8. $C_{12}H_{13}O_2NCl_2$ requires C, 49·3; H, 5·1; Cl, 24·3; N, 4·8%)].

1-*Chloro*-2 : 3-*epoxy*-4-*methoxybutane* (II). 3 : 4-Dichloro-1-methoxybutan-2-ol (34·6 g.), suspended in water (25 g.), was stirred at 30—40°, and sodium hydroxide (8 g.) in water (12 g.) added during 5 min.; stirring was continued for 1 hr. Neutralisation, extraction and recovery of the product, and distillation yielded the *epoxide* (II) (22·4 g.), b. p. 76—78°/15 mm., n_D^{20} 1·4460 (Found: C, 43·9; H, 6·7; Cl, 26·3. $C_5H_9O_2Cl$ requires C, 44·0; H, 6·6; Cl, 26·0%).

1-*Chloro*-4-*methoxybutane*-2 : 3-*diol*. 1-Chloro-2 : 3-epoxy-4-methoxybutane (21 g.) and formic acid (10 g.) were heated under reflux for 1 hr., excess of water added, and heating continued for a further hr. Final distillation gave fractions: (1) (2·4 g.), b. p. 110—117°/15 mm., n_D^{20} 1·4734; (2) (2·3 g.), b. p. 117—125°/15 mm., n_D^{20} 1·4732; and (3) (5·2 g.), b. p. 125—130°/15 mm. Fraction 1 contained some unchanged epoxide, but fraction 3 contained the glycol

[*bisphenylurethane*, m. p. 182—184° (from benzene, then aqueous alcohol) (Found: C, 58·5; H, 5·6; Cl, 9·3; N, 7·1. $C_{18}H_{21}O_5N_2Cl$ requires C, 58·1; H, 5·35; Cl, 9·05; N, 7·1%)].

1 : 2-*Epoxy*-3 : 4-*dimethoxybutane* (VI). (i) 1-Chloro-2 : 3-epoxy-4-methoxybutane (35 g.) was heated with acid methanol (50 c.c.) for 2½ hr. and worked up normally. Distillation gave a single fraction (36·2 g.), b. p. 104—105·5°/13 mm., n_D^{20} 1·4520, consisting of a mixture of 1-chloro-3 : 4- (V) and 4-chloro-1 : 3-dimethoxybutan-2-ol (VII).

(ii) Sodium hydroxide (9 g.) in water (20 c.c.) was added gradually, with stirring, to the product (35·6 g.) from (i) above, at <30°. After *ca.* 1 hr. the product yielded, on final distillation, fractions (1) (18·0 g.), b. p.[74] 62·5°/13 mm., n_D^{20} 1·4214, (2) (3·1 g.), b. p. 62·5—102·5°/13 mm., n_D^{20} 1·4270, and (3) (4·3 g.), b. p. 102·5°/13 mm., n_D^{20} 1·4478, and a residue. Fraction 1 was the required epoxide (VI) (Found: C, 53·9; H, 9·2%; epoxide equiv., 132·7. Calc. for $C_6H_{12}O_3$: C, 54·5; H, 9·1%; epoxide equiv., 132·0). Fraction 3 was found spectroscopically to consist of 4-chloro-1 : 3-dimethoxybutan-2-ol, prepared also in a different way (see below).

1-*Chloro*-3 : 4-*dimethoxybutan*-2-*ol* (V). 1 : 2-Epoxy-3 : 4-dimethoxybutane (VI) (10 g.) was treated, with cooling, with an excess of ethereal hydrogen chloride. Distillation provided 1-*chloro*-3 : 4-*dimethoxybutan*-2-*ol* (V) (10·0 g.), b. p. 101—105·5°/14 mm., n_D^{20} 1·4520 (Found: OMe, 37·2. $C_6H_{13}O_3Cl$ requires 2OMe, 36·8%), chromatographically pure [*phenylurethane*, m. p. 59—60·5° (Found: C, 54·0; H, 6·0; Cl, 12·3; N, 4·9. $C_{13}H_{18}O_4NCl$ requires C, 54·25; H, 6·3; Cl, 12·3; N, 4·9%)].

1 : 4-*Dimethoxybut*-2-*ene*. This was prepared by essentially the method of Reppe *et al.*[15] from 1 : 4-dichlorobut-2-ene (250 g.). The dimethoxybutene (176 g.), b. p. 146°/1 atm., n_D^{20} 1·4214, was found on chromatography to be a mixture of *trans*- and *cis*-isomers (72·5 : 27·5); the dichlorobutene used was a similar mixture (70 : 30).

2 : 3-*Epoxy*-1 : 4-*dimethoxybutane* (III). 1 : 4-Dimethoxybut-2-ene (65 g.) in ether (400 c.c.) and *N*-bromosuccinimide (100 g.) in water (400 c.c.) were stirred together at room temperature until the solid had disappeared (28 hr.). The crude bromohydrin, after extraction with ether and evaporation of the solvent, was stirred at *ca.* 30° for 1½ hr. with sodium hydroxide (24 g.) in water (50 c.c.). Working up gave the *epoxide* (41·9 g.), b. p. 67—70°/13 mm., n_D^{20} 1·4220 (Found: C, 54·35; H, 8·9%; epoxide equiv., 136·3. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1%; epoxide equiv., 132·0).

1 : 3 : 4-*Trimethoxybutan*-2-*ol* (IV). (i) 2 : 3-Epoxy-1 : 4-dimethoxybutane (III) (15 g.) was heated for 2 hr. with methanol (30 c.c.) containing a trace of sulphuric acid. Working up gave the *trimethoxybutanol* (15·0 g.), b. p. 98·5—99·5°/14 mm., n_D^{20} 1·4311 (Found: OMe, 56·3. $C_7H_{16}O_4$ requires 3OMe, 56·7%), chromatographically pure (3 : 5-dinitrobenzoate, m. p. 90—91°).

(ii) 1 : 2-Epoxy-3 : 4-dimethoxybutane (VI) (4·5 g.) was treated as in (i), to give 1 : 3 : 4-trimethoxybutan-2-ol (3·7 g.), b. p. 101°/13 mm., n_D^{20} 1·4311; this had an identical infrared spectrum and gave a similar 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 90·5—91·5°, to the product from the 2 : 3-epoxy-1 : 4-dimethoxybutane, above.

1 : 4-*Dichloro*-3-*methoxybutan*-2-*ol* (X). 1 : 4-Dichloro-2 : 3-epoxybutane (150 g.) and methanol (250 c.c.) containing sulphuric acid (1 c.c.) were heated under reflux overnight. Distillation of the product gave fractions (1) (1·1 g.), b. p. <110·5°/13 mm., (2) (141·8 g.), b. p. 110·5—111°/13 mm., n_D^{20} 1·4760, (3) (13·9 g.), b. p. 111—130°/13 mm., partially solid, and (4) (6·2 g.), b. p. 130—135°/13 mm., solid, and a residue (0·2 g.). Fraction 4, after recrystallisation from ethyl acetate–carbon tetrachloride, had m. p. 126—128°, undepressed on admixture with *meso*-1 : 4-dichlorobutane-2 : 3-diol. Fraction 2 was the *dichloro-methoxybutanol* (Found: C, 34·35; H, 5·9; Cl, 41·3; OH, 9·2. $C_5H_{10}O_2Cl_2$ requires C, 34·7; H, 5·8; Cl, 41·05; OH, 9·8%). By vapour-phase chromatography it was shown to contain two isomers (presumably *erythro* and *threo*) in a ratio of *ca.* 3 : 1. It yielded a *phenylurethane*, m. p. 100—102° (Found: C, 49·1, 49·2; H, 5·1, 5·4; Cl, 24·6, 23·9; N, 4·7, 5·3. $C_{12}H_{15}O_2NCl_2$ requires C, 49·3; H, 5·1; Cl, 24·3; N, 4·8%).

1-*Chloro*-3 : 4-*epoxy*-2-*methoxybutane* (XI). 1 : 4-Dichloro-3-methoxybutan-2-ol (140 g.) was stirred with aqueous sodium hydroxide solution at 30—40° for 2 hr., and on working up gave the *epoxide* (XI) (97·5 g.), b. p. 67—68°/15 mm., n_D^{20} 1·4468 (Found: C, 43·8; H, 6·6; Cl, 25·7; OMe, 23·7%; epoxide equiv., 140·3. $C_5H_9O_2Cl$ requires C, 43·95; H, 6·6; Cl, 26·0; OMe, 22·7%; epoxide equiv., 136·5). On vapour-phase chromatography the epoxide was found to be a mixture of two isomers (*ca.* 2 : 1).

[14] Blicke and Biel, *J. Amer. Chem. Soc.*, 1954, **76**, 3163.
[15] Reppe *et al.*, *Annalen*, 1955, **596**, 1.

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The epoxide (12 g.) was kept in an excess of ethereal hydrogen chloride overnight. Distillation then gave 1 : 4-dichloro-3-methoxybutan-2-ol (14·5 g.), b. p. 106°/11 mm., n_D^{20} 1·4770 (phenylurethane, m. p. and mixed m. p. 102—103°), identical spectroscopically with the precursor of epoxide (XI).

4-*Chloro*-1 : 3-*dimethoxybutan*-2-*ol* (VII). 1-Chloro-3 : 4-epoxy-2-methoxybutane (XI) (25 g.) was added gradually to boiling methanol (50 c.c.) containing sulphuric acid (5 drops); after the exothermic reaction had subsided heating was continued for 3 hr. The product was worked up, to give chromatographically pure *chlorodimethoxybutanol* (VII) (24·0 g.), b. p. 100·5—102·5°/13 mm., n_D^{20} 1·4512 (Found: OMe, 36·3. $C_6H_{13}O_3Cl$ requires 2OMe, 36·8%) {*phenylurethane*, m. p. 82—84° [from light petroleum (b. p. 60—80°)] (Found: C, 54·5; H, 6·0; Cl, 12·15; N, 4·9. $C_{13}H_{18}O_4NCl$ requires C, 54·3; H, 6·3; Cl, 12·3; N, 4·9%); 3 : 5-dinitrobenzoate, m. p. 107—109° (from methanol)}.

3-*Methoxy*-2-*methoxymethyloxetan* (IX). 4-Chloro-1 : 3-dimethoxybutan-2-ol (14 g.) was heated under reflux with sodium methoxide (from 2 g. of sodium) in methanol (40 c.c.) for 8½ hr. After working up, the *oxetan* (6·6 g.), b. p. 58—59°/13 mm., n_D^{20} 1·4233 (Found: C, 54·5; H, 9·05; OMe, 47·3. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1; 2OMe, 47·0%), was obtained, as well as some unchanged chlorodimethoxybutanol and a little trimethoxybutanol. The infrared spectrum of the oxetan showed the OMe group, and absence of unsaturation and OH groups; it had a band at 972 cm.$^{-1}$ due to the oxetan ring.[16]

Heating the oxetan (5 g.) with acid methanol (15 c.c.) gave only 1 : 3 : 4-trimethoxybutan-2-ol (4·0 g.), b. p. 94—95°/13 mm., n_D^{20} 1·4313, identified by its spectrum and 3 : 5-dinitrobenzoate.

When the oxetan (10 g.) was heated under reflux for 6 hr. with sodium methoxide solution no reaction occurred and the oxetan (8·0 g.) was recovered.

1-*Methoxybutan*-2-*ol*. This was obtained by heating 1 : 2-epoxybutane (6 g.) with sodium methoxide. The methoxybutanol (4·5 g.), b. p. 133—135°, n_D^{20} 1·4100, provided a 3 : 5-dinitrobenzoate,[17] m. p. 91·5—94° (from methanol) (Found: C, 48·65; H, 4·9; N, 9·5. Calc. for $C_{12}H_{14}O_7N_2$: C, 48·3; H, 4·7; N, 9·4%).

2-*Methoxybutan*-1-*ol*. This was similarly prepared by heating 1 : 2-epoxybutane with acid methanol. In addition to the 3 : 5-dinitrobenzoate,[17] m. p. 62—64° (from ethanol–light petroleum) (Found: C, 48·8; H, 4·7; N, 9·55%), of 2-methoxybutan-1-ol, there was also isolated the derivative of the 1-methoxybutan-2-ol from the lowest-boiling fraction of the product.

Reaction of Intermediates with Sodium Methoxide.—1-*Chloro*-2 : 3-*epoxy*-4-*methoxybutane* (II). The epoxide (II) (13·6 g.) and sodium methoxide solution (50 c.c. containing 2·88 g. of sodium) were heated at 65—70° for 3½ hr. Distillation of the product gave fractions (1) (1·4 g.), b. p. 67—74°/13 mm., n_D^{20} 1·4310, (2) (1·6 g.), b. p. 74—91·5°/13 mm., n_D^{20} 1·4361, (3) (1·6 g.), b. p. 91·5—95°/13 mm., n_D^{20} 1·4351, (4) (5·9 g.), b. p. 95—97°/13 mm., n_D^{20} 1·4338, (5) (3·1 g.), b. p. 97—98°/13 mm., n_D^{20} 1·4351, and (6) (0·5 g.), b. p. 98—100°/13 mm., n_D^{20} 1·4380, and a residue (0·3 g.). Infrared spectroscopy showed that fraction 1 contained starting material (30%) and oxetan (IX) with possibly some 2 : 3-epoxy-1 : 4-dimethoxybutane (III); fraction 2 had starting material (*ca.* 20%) and some oxetan, but mainly 1 : 3 : 4-trimethoxybutan-2-ol; fractions 3—6 were all trimethoxybutanol.

2 : 3-*Epoxy*-1 : 4-*dimethoxybutane* (III). The epoxide (III) (12 g.) was heated on the bath overnight with an excess of sodium methoxide solution. There was finally obtained 1 : 3 : 4-trimethoxybutan-2-ol (8·5 g.), b. p. 95—96°/13 mm., n_D^{20} 1·4311, identified by its spectrum and 3 : 5-dinitrobenzoate.

1 : 4-*Dichloro*-3-*methoxybutan*-2-*ol* (X). Sodium methoxide (from 3·5 g. of sodium in 50 c.c. of methanol) was added, at 20° with stirring, to 1 : 4-dichloro-3-methoxybutan-2-ol (10 g.) in methanol (10 c.c.), during 10 min. After a further ½ hour's stirring at room temperature the mixture was heated to 65—70° for 5 hr. Normal working up gave fractions (1) (4·4 g.), b. p. 57·5—59°/13 mm., n_D^{20} 1·4238, (2) (0·7 g.), b. p. 59—65°/13 mm., n_D^{20} 1·4251, and (3) (2·0 g.), b. p. 92·5—100°/13 mm., n_D^{20} 1·4423, and a residue (0·3 g.). The infrared spectra showed that fractions 1 and 2 were mainly the oxetan (IX), and fraction 3 mainly trimethoxybutanol (IV).

1-*Chloro*-3 : 4-*epoxy*-2-*methoxybutane* (XI). The epoxide (17 g.), when treated with an excess of sodium methoxide as above, gave finally fractions (1) (2·0 g.), b. p. <58°/15 mm., and (2)

[16] Ref. 6, p. 119.
[17] Bartlett and Ross, *J. Amer. Chem. Soc.*, 1948, **70**, 926.

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(8·5 g.), b. p. 58—58·5°/13 mm., n_D^{20} 1·4229, and a residue (0·7 g.). Fraction 2 (Found: OMe, 47·0. Calc. for $C_6H_{12}O_3$: OMe, 47·0%) consisted of the oxetan (IX); this was confirmed by its infrared spectrum.

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116. *Oxygen Exchange between Nitrous Acid and Water.*

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The rate of exchange of oxygen atoms between water and nitrous acid is proportional to the square of the concentration of nitrous acid. This second-order rate law corresponds to the formation of dinitrogen trioxide, with consequent oxygen exchange. The rate of formation of dinitrogen trioxide, estimated from the rate of oxygen exchange, is similar to that estimated from the rate of diazotisation of aniline.

THERE are many reactions of nitrous acid (or its esters) in which there is nucleophilic attack upon the nitrogen atom, with expulsion of a hydroxyl (or alkoxyl) group. These reactions do not occur in alkaline solution (except for the esters). Thus the nitrite ion does not exchange its oxygen atoms with water,[1] but the nitrous oxide from the decomposition of nitrous acid by hydroxylamine in $H_2{}^{18}O$ is isotopically enriched;[2] therefore there must be oxygen exchange between water and nitrous acid, or some entity derived from the latter.

There are various possible reaction paths for this exchange:

$$(1)\quad H_2\overset{+}{N}O_2 + H_2{}^{18}O \rightleftharpoons H_2\overset{+}{N}O_2{}^{18}O + H_2O$$

$$(2)\quad H_2\overset{+}{N}O_2 \rightleftharpoons \overset{+}{N}O + H_2O$$

$$(3)\quad H_2\overset{+}{N}O_2 + \overset{-}{N}O_2 \rightleftharpoons N_2O_3 + H_2O$$

Reactions analogous to (1) are the acid-catalysed hydrolyses of alkyl nitrites [3] and the acid-catalysed diazotisation of aromatic amines by the nitrous acidium ion.[4] Reaction (2) must occur in concentrated mineral acid, because the nitrosonium ion ^+NO exists in such solutions.[5] Diazotisation and deamination by dinitrogen trioxide, formed by reaction (3), are also well known.[6]

Many reactions of nitrous acid and its esters are catalysed by nucleophilic anions, so we studied the oxygen exchange of nitrous acid in the absence of such anions (with the necessary exception of nitrite). There being no net chemical change during an isotopic exchange, it is easy to control the acidity of a solution without recourse to a buffer. Here small amounts of perchloric acid were added to a large excess of sodium nitrite; the concentration of nitrous acid was then that of the added perchloric acid. Preliminary accounts of this work have been given.[7]

Various methods can be devised for following the oxygen exchange between nitrous acid and water. The simplest is to follow the changing isotopic abundance of the water.[1]

[1] Alexander and Hall, *J. Amer. Chem. Soc.*, 1940, **62**, 3455.
[2] Friedman and Bothner-By, *J. Chem. Phys.*, 1952, **20**, 459.
[3] Allen, *J.*, 1954, 1968.
[4] Hughes, Ingold, and Ridd, *J.*, 1958, 77.
[5] Angus and Leckie, *Proc. Roy. Soc.*, 1935, *A*, **149**, 327; **150**, 615; Bayliss and Watts, *Austral. J. Chem.*, 1956, **9**, 319; Singer and Vamplew, *J.*, 1956, 3971; Gillespie and Millen, *Quart. Rev.*, 1948, **2**, 277.
[6] (*a*) Hughes, Ingold, and Ridd, *J.*, 1958, 65, 70, 88; (*b*) Taylor, *J.*, 1928, 1099, 1897.
[7] Bunton, Llewellyn, and Stedman, *Nature*, 1955, **175**, 83; *Chem. Soc. Spec. Publ.*, 1957, No. 10, 113.

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Alternatively, the nitrous acid can be decomposed *in situ* by reagents such as hydroxylamine [7] or hydrazoic acid [8] to a gas, *e.g.*, nitrous oxide, which can be analysed mass spectrometrically. As control tests on the azide method showed that some oxygen of the nitrous oxide came from the water during decomposition, we did not use this method, although others have used it successfully.[8] Our usual method was the isolation of nitrous acid as its silver salt, and decomposition of this to water by heating it with ammonium chloride. The first method, analysis of the solvent water, was used for a few experiments. The concentration of nitrite was varied between 0·4 and 3M.

At 0° in water, the rate of exchange R was proportional to the square of the nitrous acid concentration, and independent of the stoicheiometric concentration of nitrite (Table 1),

TABLE 1. *Oxygen exchange between nitrous acid and water at* 0°.

$10[HNO_2]$ (M)	[Nitrite] (M)	10^3R (mole l.$^{-1}$ sec.$^{-1}$)	$10R/[HNO_2]^2$ (l. mole^{-1} sec.$^{-1}$)	$10[HNO_2]$ (M)	[Nitrite] (M)	10^3R (mole l.$^{-1}$ sec.$^{-1}$)	$10R/[HNO_2]^2$ (l. mole^{-1} sec.$^{-1}$)
0·118	0·555	0·0582	4·2	0·541	1·995	1·34	4·6
0·133	0·412	0·104	5·8	0·561	1·087	1·41	4·5
0·258	0·410	0·410	6·2	0·561	0·517	1·71	5·4
0·258	0·655	0·297	4·5	0·792	0·591	3·80	6·0
0·264	0·536	0·319	4·6	1·13	0·457	7·46	5·8
0·287	1·134	0·368	4·5	0·177 *	2·76	0·173	5·5
0·352	1·162	0·575	4·7	0·0765 †	1·40	0·294	50
0·376	0·534	0·796	5·6	0·231 †	1·40	3·55	67

Mean $R/[HNO_2]^2 = 0·51$ (l. mole^{-1} sec.$^{-1}$) at 0°.

* Method 2 used. † 25·0°.

i.e., $R = k_{ex}[HNO_2]^2$. Therefore the most plausible scheme for this exchange (in the absence of other anions) is:

$$2HNO_2 \rightleftharpoons H_2\overset{+}{N}O_2 + \dot{\overset{-}{N}}O_2 \text{ (fast)}; \quad H_2\overset{+}{N}O_2 + \overset{-}{N}O_2 \rightleftharpoons N_2O_3 + H_2O$$

Paths (1) and (2) would give the law

$$R = k[H^+][HNO_2] \approx k'[HNO_2]^2/[NO_2^-]$$

These paths cannot be major mechanistic components because of the independence of rate of the concentration of nitrite ion. They may be important in conditions other than those used here.

Our solutions always contained perchlorate ion from the acid, and small amounts of nitrate ion from the added nitrite. Addition of small amounts (<0·1M) of these ions did not affect the exchange rates (Table 2).

TABLE 2. *Effect of added salts of strong acids* (Method 1).

	Added salt (M)	$10[HNO_2]$ (M)	[Nitrite] (M)	10^3R (mole l.$^{-1}$ sec.$^{-1}$)	Rate increase (%)
$NaClO_4$	0·072	0·302	0·601	0·451	−3
,, ...	1·02	0·500	0·819	2·21	41
$NaNO_3$	0·055	0·245	0·555	0·251	−17
,, ...	0·197	0·451	0·620	1·00	−4
,, ...	1·32	0·257	0·829	0·487	42
,, ...	1·37	0·537	0·564	2·43	62
NaCl	2·16	0·240	0·788	0·657	119
,, ...	2·21	0·354	0·762	1·39	114
NaBr	1·02	0·190	0·660	0·315	68
,, ...	1·21	0·184	0·661	0·352	99
KCNS	1·45	0·211	0·796	0·415	79

Comparison with the Hydrolysis of Alkyl Nitrites.—The exchange of oxygen between water and carboxylic acids is analogous to hydrolysis of their esters, so we might expect a similar correspondence between nitrous acid exchange and alkyl nitrite hydrolysis. The mechanism of the acid hydrolysis of alkyl nitrite is a bimolecular attack of water upon the

[8] Anbar and Taube, *J. Amer. Chem. Soc.*, 1954, **76**, 6243.

conjugate acid of the ester.[3] We have not observed this mechanism for the oxygen exchange of nitrous acid. This is not necessarily because it does not exist; it may be that, with the large concentration of nitrite ion used the bulk reactivity of nitrite ions towards nitrous acidium ion is much greater than that of water. From the known rates of hydrolyses of alkyl nitrites we can calculate the relative reactivities of halide ions and water towards a protonated alkyl nitrite. For *n*-propyl nitrite in aqueous dioxan $k_{H_2O}/k_{Br^-} \approx 5 \times 10^{-4}$, and because nitrite and bromide ions have similar reactivities towards the nitrous acidium ion [6a,9] the ratio $k_{H_2O}/k_{NO_2^-}$ for attack upon the protonated ester is probably not very different. If the relative reactivities of nitrite ion and water towards the nitrous acidium ion and protonated ester are similar it will therefore be possible to observe exchange *via* bimolecular attack of water as an isolated mechanism only when the concentration of nitrite ion is much less than that used here.

Comparison with Diazotisation.—In many reactions dinitrogen trioxide is the reactive intermediate, and for some of these, *e.g.*, the diazotisation of aniline, its formation can be rate-determining.[6a] Then the kinetic form becomes Rate $= k''_2[HNO_2]^2$. The two measurements were made under very different conditions (for diazotisation $[NO_2^-] \approx 10^{-3}$M) and the estimated value [6a] of k''_2 (but not of k_{ex}) depends upon the value taken for the dissociation constant of nitrous acid. Within these limitations there is fair agreement between k_{ex} and k''_2, *e.g.*, at 0° in water, $k_{ex} = 0{\cdot}51$ (l. mole^{-1} sec.$^{-1}$) [$k''_2 \approx 0{\cdot}8$ (l. mole^{-1} sec.$^{-1}$)].

Effect of Added Anions.—Added anions, X^-, may affect the rate of exchange in two ways: (*a*) they may have a primary or secondary salt effect, or (*b*) they may provide a new path for oxygen exchange, *e.g.*,

$$H_2\overset{+}{N}O_2 + \bar{X} \rightleftharpoons NOX + H_2O$$

The second mode must play a part whenever the bulk reactivity of the added anion towards the nitrous acidium ion is comparable with that of the nitrite ion.

Anions of Weak Acids.—In solutions of nitrous acid buffered with phosphate or carboxylate ions attack of these highly nucleophilic anions may swamp the uncatalysed attack of nitrite ion. Then the rate of exchange will be of the first order with respect to nitrous acid, and will depend upon the nature and concentration of the buffer. This seems to occur with acetate buffers, because here the rate of exchange, at a given pH, is approximately proportional to the first, not the second, power of the nitrite concentration

TABLE 3. *Exchange in acetate buffer at* 25° (Method 2).

[Nitrite] (M)	[$CH_3 \cdot CO_2Na$] (M)	[$CH_3 \cdot CO_2H$] (M)	pH *	10^4R (mole l.$^{-1}$ sec.$^{-1}$)
0·560	3·92	1·48	5·32	4·7
1·61	3·79	1·44	5·36	10·3

* Measured with a glass electrode.

TABLE 4. *Thiocyanate-catalysed diazotisation of aniline at* 0°.

10^3[$PhNH_2$,$HClO_4$] (M)	0·98	3·93	0·98	0·98	1·97
10^3[H^+] (M)	2·57	2·57	2·57	3·17	6·14
10^3{[HNO_2] + [NO_2^-]} (M)	1·00	1·00	1·00	0·40	1·00
10^4[$C\bar{N}S$] (M)	9·41	9·41	3·76	9·41	3·76
10^6 × Instantaneous rate	2·55	2·55	1·33	0·82 *	2·75
$10^{-3}k_2^{CNS}$	1·37	1·37	1·54	1·45	1·55

* Instantaneous rates were calculated at a point of the run corresponding to 10^4 [HNO_2] = 6·67M, except for run *; here the rate refers to 10^4 [HNO_2] = 1·82M.

(Table 3 and ref. 7). Such a catalysis almost certainly also occurs with phosphate buffers, although it is here complicated by the coexistence of mono- and di-anions, which will have different reactivities towards the nitrous acidium ion.

[9] Hughes, Ingold, and Ridd, *J.*, 1958, 82.

Effect of Anions of Strong Acids.—Halide ions catalyse diazotisation, and the acid hydrolysis of alkyl nitrites, by introducing new paths, *viz.*,

$$H_2\overset{+}{N}O_2 + \bar{B}r \rightleftharpoons NOBr + H_2O; \quad RO\overset{+}{N}OH + \bar{C}l \rightleftharpoons NOCl + ROH$$

The nitrosyl halide then reacts with a nucleophilic reagent, *e.g.*, water or amine.[9] The relative reactivities of halide and nitrite ions towards the nitrous acidium ion can be calculated from rates of diazotisation [6a,9] (in the Experimental section we give results on rates of diazotisation which give an estimate of the relative reactivity of the thiocyanate ion also). These diazotisations are made at low ionic strengths, where specific salt effects are relatively unimportant. Nucleophilic anions (*e.g.*, Br^-, CNS^-) catalyse diazotisation, but the weakly nucleophilic anions (*e.g.*, NO_3^- and ClO_4^-) have little effect when in low concentration. In principle it should be possible to do similar experiments on oxygen exchange. Unfortunately our experimental methods required concentrations of nitrite ion $>0{\cdot}4$M, and so to get an accurately measurable increase in rate it was necessary to use even higher concentrations of the added salt. Preliminary experiments showed that such high salt concentrations had a marked effect on diazotisation, and this has since been confirmed by a more detailed study.[10]

Added sodium perchlorate, nitrate, bromide, and chloride and potassium thiocyanate (1—2M) increased the rate of oxygen exchange, *e.g.*, the rate was doubled in the presence of 2M-sodium chloride (Table 2). These effects depended upon the nature and concentration of the added salt. The sequence was: $NaBr > KCNS \approx NaCl > NaClO_4 > NaNO_3$. These rate increases could be caused by either a chemical intervention, or specific salt effects, or both. It did not seem possible to separate these effects at the high salt concentrations used.

Sodium nitrite itself appears to have no specific salt effect upon the rate of exchange, which is unaffected by an eightfold change in the concentration of sodium nitrite (Table 1). We therefore think that the rates of diazotisation and oxygen exchange can be compared despite the considerable differences in the concentration of nitrite ion.

The rate of dehydration of nitrous acid to dinitrogen trioxide can be written as:

$$\text{Rate} \propto [HNO_2]^2 f^2_{HNO_2}/f^*$$

(where f_{HNO_2} and f^* are the activity coefficients of nitrous acid and the transition state respectively).

We might expect the activity-coefficient term to cancel out, because the transition state is made up of two molecules of nitrous acid. This seems to be so when sodium nitrite is the only salt present in high concentration. However, salt effects are often highly specific, and it may be that the term $f^2_{HNO_2}/f^*$ will change when salts other than sodium nitrite are present in large amounts. f_{HNO_2} changes only slowly with ionic strength,[11] and so variation in the activity coefficient term is probably largely due to changes in f^*.

Experimental

Kinetic Methods for Isotopic Exchange.—(1) *Determination of isotopic abundance of nitrous acid.* Decomposition of isotopically normal nitrous acid in $H_2{}^{18}O$ by hydrazoic acid or hydroxylamine gave some tracer in the nitrous oxide; the amount depended upon the conditions used. It seems, however, that the azide method can give reproducible results under standard conditions (cf. ref. 8). Decomposition of the nitrous acid, or its salts, to nitric oxide was not a satisfactory method, in part because the gas causes difficulties in mass spectrometry.[12]

Therefore the nitrous acid was isolated as its sparingly soluble silver salt, and this was decomposed: $AgNO_2 + NH_4Cl \longrightarrow N_2 + 2H_2O + AgCl$. The water was equilibrated with carbon dioxide and this gas analysed mass spectrometrically. (This method could not be used when a salt or acid giving an insoluble oxygen-containing silver salt was present.)

[10] Challis and Ridd, personal communication.
[11] Abel and Neusser, *Monatsh.*, 1929, **53**, 855.
[12] Bigeleisen, *J. Amer. Chem. Soc.*, 1952, **74**, 4944.

The nitrous acid solutions were covered with a layer of purified heptane; this greatly decreased the rate of decomposition of the nitrous acid. Sodium nitrite, sometimes with another salt, in $H_2{}^{18}O$, was cooled to 0°, and oxygen and carbon dioxide were removed in a stream of nitrogen. The required amount of ice-cold perchloric acid was then added (nitric acid was used when potassium thiocyanate was present). At suitable times, portions were removed and added to *a* slight excess of aqueous ammonia (s.g. 0·880). An aliquot part was removed and titrated with standard alkali, in the absence of carbon dioxide, with Thymol Blue indicator. (All solution transfers were made with pre-cooled pipettes.) The excess of ammonia was pumped off from the samples, and silver nitrate added. The washed silver nitrite precipitate was dried *in vacuo* (P_2O_5), then ground with dried ammonium chloride, and all volatile matter was pumped off at room temperature. The mixture was decomposed *in vacuo* at 220°. The evolved water distilled out, and was purified by static distillation. This purified water was then isotopically analysed by means of equilibrated carbon dioxide. A correction was applied for the isotopic dilution by the oxygen atoms of the carbon dioxide.

We tested the validity of this method. (1) Isotopically normal sodium nitrite was added to ammonia in $H_2{}^{18}O$. The isolated silver nitrite contained no tracer. (2) Silver nitrite did not exchange with $H_2{}^{18}O$ either in the presence or absence of silver nitrate. (3) An isotopic dilution experiment showed that no significant amounts of tracer were introduced *via* the reagents. (4) The isotopic abundance of the nitrite, found and calculated for complete exchange, agreed within 5%. This difference may be due to adventitious loss of tracer, or to isotopic fractionation. The value of isotopic abundance for complete exchange, N_∞, was taken as that calculated from the isotopic abundance of the water, and the relative amounts of water and sodium nitrite.

(2) *Determination of the changing abundance of the water.* Isotopically enriched sodium nitrite was prepared by equilibration with $H_2{}^{18}O$ containing a trace of nitric acid. After several days the water was pumped off, and the salt dissolved in normal water, and redried *in vacuo*. This was repeated. The dried and powdered salt, stored *in vacuo* (P_2O_5), contained more than 99·5% of sodium nitrite (w/w). Solutions of this enriched salt were made up with isotopically normal water containing perchloric acid or acetate buffer, as for Method 1. At intervals samples were removed, and the exchange stopped by addition of a small known amount of sodium hydroxide. The water was pumped off and analysed by use of equilibrated carbon dioxide. Corrections were made for isotopic dilutions during analysis. This method was used for a run with phosphate buffer (0·05M, pH 5·39) and 0·664M-sodium nitrite at 25°; 10^5R = 4·0 (mole $l.^{-1}$ $sec.^{-1}$). This value is close to that found by Anbar and Taube [8] for exchange in a similar buffer (pH 5·47) and 0·50M-sodium nitrite, *viz.*, $10^5R = 3·5$ (mole $l.^{-1}$ $sec.^{-1}$).

Calculation of Results.—The exchange rate R was calculated from:

$$R = \frac{2[\text{nitrite}][H_2O]}{2[\text{nitrite}] + [H_2O]} \cdot \frac{d \log_e (N_\infty - N_t)}{dt}$$

N_t and N_∞ are the isotopic abundances in excess at time t and for complete exchange respectively.

Exchange in $H_2{}^{18}O$. [Nitrite] = 0·591M. [HNO_2] = 0·0792M. 0°

Time (min.)	1·50	3·06	5·03	7·50	∞		
N (atoms % excess)	0·434	0·515	0·738	0·834	1·066	1·049	1·063*

* Calc. from N_{H_2O}.

10^5R = 3·80 moles $l.^{-1}$ $sec.^{-1}$; $R/[HNO_2]^2$ = 0·603 l. $mole^{-1}$ $sec.^{-1}$.

Exchange with $NaNO^{18}O$. [Nitrite] = 1·40M. [HNO_2] = 0·023M. 25°.

Time (min.)	1·14	2·02	3·02	5·58	8·03	∞		
N (atoms % excess)	0·027	0·029	0·042	0·090	0·098	0·242	0·241	0·242

10^3R = 3·55 moles $l.^{-1}$ $sec.^{-1}$; $R/[HNO_2]^2$ = 6·68 l. $mole^{-1}$ $sec.^{-1}$.

Appendix.—Catalysis of diazotisation by thiocyanate ion. It was found that potassium thiocyanate (*ca.* M) increased the rate of oxygen exchange between nitrous acid and water (Table 2). This could be a salt effect, or the result of the new reaction path:

$$CNS^- + HNO_2{}^+ \rightleftharpoons NO{\cdot}CNS + H_2O$$

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Nitrosyl thiocyanate might well be a nitrosating agent, as are the nitrosyl halides. Therefore the diazotisation of aniline was studied with added potassium thiocyanate at 0° in water, following the procedures already described.[4, 6a, 9]

In the absence of added thiocyanate ion the rate equation is $v = k''_2[HNO_2]^2$, corresponding to the rate-determining formation of dinitrogen trioxide.[6a] Addition of thiocyanate ion increased the rate, which was independent of a change in concentration of amine from 0·01M to 0·04M. A series of experiments were made with different reagent concentrations (Table 4). Instantaneous rates were calculated by drawing tangents to the concentration–time curve at *ca.* 20% reaction. These were corrected for the uncatalysed rate of diazotisation through dinitrogen trioxide, the dissociation constant of nitrous acid being taken as $3·2 \times 10^{-4}$ mole l.$^{-1}$ at 0°, to give the rate of formation of nitrosyl thiocyanate $= k_3^{CNS}[H^+][HNO_2][C\bar{N}S]$. From these figures, $10^5 k_3^{CNS} = 1·5$ l.^{2} mole^{-2} sec.$^{-1}$ for the overall reaction:

$$\overset{+}{H} + HNO_2 \rightleftharpoons H_2\overset{+}{N}O_2$$

$$H_2\overset{+}{N}O_2 + C\bar{N}S \xrightarrow[\text{slow}]{} NOCNS + H_2O$$

$$NOCNS + PhNH_2 \xrightarrow[\text{fast}]{} Ar\overset{+}{N}_2 + H_2O + C\bar{N}S$$

and k_3^{CNS} is a measure of the reactivity of the thiocyanate towards the nitrous acidium ion. Its value is very similar to those found for the iodide ($10^5 k_3^I = 1·4$ l.^{2} mole^{-2} sec.$^{-1}$) and bromide ions ($10^5 k_3^{Br} = 1·2$ l.^{2} mole^{-2} sec.$^{-1}$).[9]

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117. *The Hemicelluloses of Loblolly Pine* (Pinus taèda) *Wood. Part II.* The Constitution of Hexosan and Pentosan Components.*

By J. K. N. JONES and T. J. PAINTER.

A copper-complexing hemicellulose fraction (I) from loblolly pine wood has been divided into a subfraction (II) containing residues of galactose, glucose, and mannose in the ratio 1 : 7 : 19, and a subfraction (III) containing residues of xylose and 4-*O*-methylglucuronic acid in the ratio 6 : 1.

Hydrolysis of methylated (II) yielded 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose (1 part), 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose (1 part), the 2 : 3 : 6-tri-*O*-methyl ethers of D-mannose and D-glucose (30 parts), and di-*O*-methyl hexoses (*ca.* 1 part).

Hydrolysis of methylated (III) gave 2 : 3 : 4-tri-*O*-methyl-D-xylose (3 parts), 2 : 3-di-*O*-methyl-D-xylose (60 parts), 3-mono-*O*-methyl-D-xylose (3 parts), 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid (1 part), and 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-α-D-glucuronosyl)-D-xylose (10 parts). These and other results are discussed.

PART I of this series described the isolation from loblolly pine (*Pinus taèda* L.) wood of a hemicellulose fraction (I) containing residues of galactose, glucose, mannose, xylose, and 4-*O*-methylglucuronic acid. Structural features of its constituent polysaccharides were discussed in the light of partial acid-hydrolysis. A similar hemicellulose fraction has now been divided into a subfraction (II) containing residues of galactose, glucose, and mannose only, and a subfraction (III) containing residues of xylose and 4-*O*-methylglucuronic acid only.

Addition of Fehling's solution to an alkaline extract of loblolly pine sawdust yielded

* Part I, Jones and Painter, *J.*, 1957, 669.

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an insoluble copper-complex, from which the hemicellulose fraction (I) was regenerated. Acetylation of this fraction with acetic anhydride and anhydrous zinc chloride yielded a mixture of polysaccharide acetates, which was dissolved in chloroform. Agitation of this solution with ice-cold, aqueous sodium carbonate caused part of it to form a stable emulsion, which was separated. From the remaining chloroform solution, a mixture of neutral polysaccharide acetates was recovered, and deacetylated to yield subfraction (II). Acidification of the emulsion, followed by extraction with chloroform, led to the recovery of a mixture of acidic polysaccharide acetates, which was deacetylated to yield subfraction (III).

Subfraction (II) had $[\alpha]_D$ — 20° in dilute alkali, and during hydrolysis with aqueous formic acid, the specific rotation (calculated as anhydrohexose) rose from —21° to a constant value of +21° in 10 hr. The hydrolysate was separated chromatographically into galactose, glucose, and mannose components; estimation of these by periodate oxidation [1] indicated that they were present, respectively, in the ratio 1 : 7 : 19.

On periodate oxidation, subfraction (II) consumed 1·02 moles of periodate per anhydrohexose unit, with the concomitant liberation of 0·133 mole of formic acid. Electrophoresis of the material on fibre-glass sheets [2] caused it to travel as a single, elongated spot, which was located by the method of Cifonelli and Smith.[3] The intrinsic viscosity of a solution of subfraction (II) in M-cupriethylenediamine was 0·12 dl./g.

Subfraction (III) had $[\alpha]_D$ —20° in dilute alkali, and yielded three sugars when hydrolysed with dilute sulphuric acid. These were chromatographically indistinguishable from xylose, 4-*O*-methylglucuronic acid, and 2-*O*-(4-*O*-methyl-α-D-glucuronosyl)-D-xylose. Iodometric titration of the three sugars indicated that subfraction (III) contained residues of xylose and 4-*O*-methylglucuronic acid respectively in the ratio 6 : 1.

The fully methylated derivatives of subfractions (II) and (III) were prepared as follows. Hemicellulose fraction (I) was methylated first by prolonged exposure to diazomethane, and then with methyl sulphate and alkali. The partly methylated product (OMe, 33%) was dissolved in aqueous alkali, and the solution was extracted with chloroform. The extract contained a small proportion of methylated pentosan (furfuraldehyde test), which was removed by the selective emulsification procedure described above, to furnish pure, partly methylated (II). The remaining alkaline solution was acidified and extracted again with chloroform, to furnish pure, partly methylated (III). Remethylation of the two products separately then gave the two fully methylated derivatives.

After hydrolysis with aqueous formic acid, the specific rotation of methylated (II) rose from —18·0° to a constant value of approximately +10°. The hydrolysate was resolved into four chromatographically distinct fractions (*a*, *b*, *c*, and *d* respectively) on filter-paper sheets. Fractions *a* and *b* contained the 2 : 3 : 4 : 6-tetra-*O*-methyl ethers of D-mannose and D-galactose respectively; these were characterised by conversion into their corresponding *N*-phenylglycosylamines. Fraction *c* could not be readily resolved on paper chromatograms, but application of selective methyl furanoside formation according to Reberr and Smith's directions [4] led to the isolation of 2 : 3 : 6-tri-*O*-methyl-D-mannose and 2 : 3 : 6-tri-*O*-methyl-D-glucose from this fraction; these sugars were characterised as their 1 : 4-di-*O*-*p*-nitrobenzoates. Fraction *d* consisted of a mixture of di-*O*-methylhexoses, none of which was positively identified. By weighing the respective fractions after isolation, it was estimated that *a*, *b*, *c*, and *d* were present in the approximate ratio 1 : 1 : 30 : 1.

The number-average molecular weight of methylated (III) was estimated, by osmometry, to be 13,550 ± 400. When hydrolysed with aqueous formic acid, the specific rotation of the material rose from —56·8° to an almost constant value of +34·4°. On chromatograms, the hydrolysis products travelled as three neutral spots (*a'*, *b'*, *c'* respectively) and two acidic spots (*d'* and *e'* respectively). After separation on filter paper sheets, *a'* was

[1] Hirst and Jones, *J.*, 1949, 1659.
[2] Bourne, Foster, and Grant, *J.*, 1956, 4311.
[3] Cifonelli and Smith, *Analyt. Chem.*, 1954, **26**, 1132.
[4] Rebers and Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 6097.

identified as 2 : 3 : 4-tri-*O*-methyl-D-xylose by conversion into its corresponding *N*-phenylglycosylamine; *b'* was obtained as crystalline 2 : 3-di-*O*-methyl-D-xylose, and *c'* afforded crystalline 3-mono-*O*-methyl-D-xylose.

Component *d'* was chromatographically indistinguishable from 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid; owing to its low yield, it was characterised in admixture with component *e'* as follows. The two sugar acids were together converted into their methyl glycosides/methyl esters with methanolic hydrogen chloride, and then reduced with lithium aluminium hydride in ether. A portion of the products, on hydrolysis, yielded 2 : 3 : 4-tri-*O*-methyl-D-glucose, identified as its crystalline aniline derivative, and 3-mono-*O*-methyl-D-xylose, tentatively identified by its electrophoretic mobility and by comparison of its infrared absorption spectrum with that of an authentic specimen. A further portion of the products was fully methylated with Purdie's reagents, and then hydrolysed, to yield 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, characterised as its crystalline aniline derivative, and 3 : 4-di-*O*-methyl-D-xylose, characterised by conversion into crystalline 3 : 4-di-*O*-methyl-D-xylonolactone. It followed that component *d'* was 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid, and that *e'* was 3-*O*-methyl-2-*O*-(2 : 3 : 4-tri-*O*-methyl-D-glucuronosyl)-D-xylose.

Iodometric titration of *a'*, *b'*, *c'*, *d'*, and *e'* indicated that they were present in the hydrolysate, respectively, in the approximate ratio 3 : 60 : 3 : 1 : 10.

These and previous results [5,6] show that the hemicelluloses of loblolly pine wood which form copper complexes contain two chemically distinct groups of polysaccharides. The hexosan group, represented by subfraction (II), is made up of essentially linear chains of D-mannose and D-glucose residues, linked through positions 1 and 4 in the β-configuration. In the particular hexosan fraction here studied (II), these chains bear, on an average, two non-reducing end-groups for every 27—33 anhydrohexose units; one of these is a D-mannopyranose residue, and the other a D-galactopyranose residue.

The isolation of about 3% of di-*O*-methylhexoses from the hydrolysate of methylated (II) probably arose from under-methylation of the polymer, or from demethylation during hydrolysis. However, the possibility that the chains contain a single branching point for every 27—33 anhydrohexose units cannot be excluded. The consumption by subfraction (II) of 1·02 moles of periodate per anhydrohexose residue is consistent with an essentially linear structure for the hexosans, but the liberation of 4 moles of formic acid for every 30 anhydrohexose residues is also consistent with slight branching of the chains. The average molecular weight of methylated (II) was too low to permit a satisfactory determination by osmometry, and viscosity data are very difficult to interpret. However, on the basis of experience with other mannoglucans, the intrinsic viscosity of subfraction (II) is believed to indicate an average D.P. of 20—30 for the hexosans.

The pentosan group of polymers is based on essentially linear chains of xylose residues, linked through position 1 and 4 in the β-configuration. In the particular fraction described here (III), all of these chains bear single terminal side-chains of 4-*O*-methyl-D-glucuronic acid residues, linked to position 2 of occasional xylose residues (1 in every 6—7), probably in the α-configuration. No neutral pentosan could be present in subfraction (III), since the acidity of the xylans formed the basis of their separation from (II) by the selective emulsification procedures.

If the xylans in subfraction (III) are considered as consisting of repeating units of 7 xylose residues and one 4-*O*-methylglucuronic acid residue, the number-average molecular weight of methylated (III) indicates an average of about 10 such repeating units per molecule, or a number-average D.P. of 85 ± 3. When considered together with the relative yields of the hydrolysis products of methylated (III), this figure indicates that the xylan skeletons contain, on an average, two branching points per molecule. From the identity of the major mono-*O*-methyl-D-xylose component (in *c'*) it appears that this branching takes place principally through position 2 of separate xylose residues.

[5] Ball, Jones, Nicholson, and Painter, *TAPPI*, 1956, **39**, 438.
[6] Jones and Painter, *J.*, 1957, 669.

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It is improbable that either subfraction (II) or (III) is a homogeneous polysaccharide. The electrophoretic behaviour of the former suggests that it contains a mixture of different yet closely related polymers. Since partial hydrolysis of fraction (I) affords substantial quantities of glucosidomannose and mannosidoglucose,[6] it is evident that heteropolymer mannoglucans must represent a major part of subfraction (II): the manner in which the galactopyranosyl end-groups are distributed in it is not known; they may be attached to mannoglucan chains, or they may be present as separate mannogalactans. The apparent absence [6] of cellulose in the partial hydrolysate of fraction (I) indicates a paucity in subfraction (II) of contiguous glucose residues, and hence of separate glucan homopolymers. Subfraction (III) probably contains a mixture of closely related 4-*O*-methylglucuronoxylans, differing in their degree of branching and in the extent to which they bear uronic acid side-chains.

Hemicelluloses of the mannoglucan type have now been isolated from a number of other softwoods, including those of western hemlock,[7,8] white spruce,[9] Sitka spruce,[10,11] Norwegian spruce,[12,13] and western red cedar,[14] and important contributions in this field have been made by Aspinall,[10] Dutton,[11] Hamilton,[7,8,14] Lindberg,[12,13] Timell,[9] Wise,[15] and their co-workers. The pentosans of coniferous woods have received less attention, but detailed structural studies have been made of those in western hemlock,[16] Norwegian spruce,[17] and European larch [18] by Dutton and Smith,[16] and by Aspinall and his collaborators.[17,18]

In the case of loblolly pine, hexosans and pentosans of the types represented by subfractions (II) and (III) appear exclusively in the fraction of the hemicelluloses forming copper complexes. Although they constitute the main bulk of the non-cellulosic polysaccharides in the wood, smaller amounts of quite different polysaccharides are present and appear in fractions which do not form copper complexes. They include a group of xylans which bear unmethylated uronic acid residues, and polymers of the arabogalactan type.[5]

Experimental

Paper chromatography was carried out on Whatman No. 1 filter paper, with the following solvent systems: (*a*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4), (*b*) butan-1-ol–ethanol–water (40 : 11 : 19), (*c*) butan-1-ol–pyridine–water (10 : 3 : 3), and (*d*) butan-2-one–water (89 : 11) (all v/v). Sugars were located on the chromatograms by spraying with a solution of *p*-anisidine hydrochloride in butan-1-ol.[19]

Unless otherwise stated, optical rotations were determined for aqueous solution at 23° ± 3°, and the figures given are equilibrium values. Solutions were concentrated under diminished pressure.

X-Ray powder diffraction photographs were taken with Cu-K_α radiation (nickel filter). The powdered samples (*ca.* 1 mg.) were mounted in the camera on silica threads, to which they were attached with Vaseline petroleum jelly. Infrared absorption spectra were recorded on a Perkin-Elmer Model 21 instrument in conjunction with potassium bromide pellets, or with 10% w/v chloroform solutions in sodium chloride cells (0·1 mm.). Scanning was carried out between 4000 and 600 cm.$^{-1}$.

Preparation and Fractionation of Hemicelluloses forming Copper Complexes.—The hemicellulose fraction (I) forming copper complexes was prepared as previously described, but

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[12] Lindberg and Meier, *Svensk Papperstidn.*, 1957, **60**, 785.
[13] Lindberg and Croon, *Acta Chem. Scand.*, 1958, **12**, 457.
[14] Hamilton and Partlow, *J. Amer. Chem. Soc.*, 1958, **80**, 4880.
[15] Merler and Wise, *TAPPI*, 1958, **41**, 80.
[16] Dutton and Smith, *J. Amer. Chem. Soc.*, 1956, **78**, 2505, 3744.
[17] Aspinall and Carter, *J.*, 1956, 3744.
[18] Aspinall and McKay, *J.*, 1958, 1059.
[19] Hough, Jones, and Wadman, *J.*, 1950, 1702.

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without prior delignification of the sawdust.[6] The yield from 850 g. of wood was 9 g. Chromatography of a sample hydrolysed by 2N-sulphuric acid at 100° for 24 hr. indicated the presence of galactose, glucose, mannose, xylose, and 4-*O*-methylglucuronic acid.

The hemicellulose (I) (5·0 g.) was dried *in vacuo* at room temperature over silica gel (3 days), then mixed with finely ground anhydrous zinc chloride (1 g.). Acetic anhydride (100 ml.) was added, and the mixture heated at 80° for 4 hr. The resulting homogeneous solution was concentrated to 50 ml. and poured into ice-cold water (1 l.). The gelatinous precipitate was collected and washed by decantation, and then dissolved in chloroform (200 ml.). The solution was dried (Na_2SO_4) and filtered through decolourising charcoal (1 cm.), agitated with ice-cold N-sodium carbonate (1 l.) in a macerator (3 min.), poured into a separatory funnel, and set aside. The homogeneous chloroform layer which separated was removed and again agitated twice in the same way. It was finally washed with water, dried (Na_2SO_4), and poured into light petroleum (1 l.).

The cream-coloured precipitate was collected (centrifuge), washed with light petroleum, and air-dried. The product (1·5 g.) had $[\alpha]_D$ − 8·9° (*c* 0·9 in acetone) (Found: Ac, 44·2. Calc. for hexosan triacetate: Ac, 44·8%). It was deacetylated in acetone solution by the addition of methanolic sodium methoxide; the precipitated polysaccharides were collected by filtration, washed with methanol, then with acetone, and air dried. A portion of the product [subfraction (II)] was hydrolysed with 2N-sulphuric acid at 100° for 24 hr.; chromatography of the hydrolysate (solvent *b*) indicated the presence of galactose, glucose, and mannose only.

The upper layer in the separatory funnel consisted of a stable emulsion; it was washed by shaking it twice with chloroform, acidified, and shaken with chloroform (500 ml.), whereupon it collapsed to yield a homogeneous chloroform layer. The latter was separated, washed with water, dried (Na_2SO_4), concentrated to 100 ml., and poured into light petroleum (500 ml.). The precipitated material was collected, washed, and dried as before. The product (0·8 g.) had $[\alpha]_D$ − 45° (*c* 0·5 in acetone) (Found: Ac, 35·2. Calc. for pentosan diacetate: Ac, 39·8%). It was deacetylated as before to yield subfraction (III). Hydrolysis of a sample, followed by chromatography (solvent *a*), indicated the presence of xylose, 4-*O*-methylglucuronic acid, and 2-*O*-(4-*O*-methylglucuronosyl)xylose.

Preliminary Examination of Subfraction (II).—The unsubstituted material had $[\alpha]_D$ − 20° (*c* 1·0 in 0·1N-NaOH). A portion (76 mg.) was heated in 50% v/v formic acid (10 ml.) at 90°. The specific rotation (calc. as anhydrohexose) rose from −21° to +21° (const.) during 10 hr. The hydrolysate was concentrated to a syrup, which was then heated in N-sulphuric acid (10 ml.) at 90° for 30 min. The solution was cooled, neutralised with Amberlite resin IR-45, and concentrated to a syrup (60 mg.). The syrup (30 mg.) was resolved into galactose, glucose, and mannose components on a paper chromatogram (30 × 40 cm.) developed in solvent *c* during 3 days with intermediate drying. Their relative amounts were determined by the method of Hirst and Jones,[1] a correction being applied for carbohydrates extracted from the paper. A ratio for galactose : glucose : mannose of 1 : 7 : 19 was indicated.

Time (hr.)	3	6	12	36	108	300
IO_4^- (mole/162 g.)	0·452	0·536	0·732	0·748	1·016	1·016
$H{\cdot}CO_2H$ (mole/162 g.)	0·060	0·064	0·079	0·095	0·111	0·133

In the periodate oxidation of subfraction (II), 250 mg. samples were suspended in 0·025M-sodium metaperiodate (250 ml.), in which they largely dissolved. Aliquot parts were withdrawn periodically for the estimation of periodate uptake, by iodometric titration, and of formic acid liberated, by titration with base.

Electrophoresis of subfraction (II) was carried out on fibre-glass sheets [2] (10 × 40 cm.) with 0·2M-sodium borate as the electrolyte. A potential difference of 600 V was applied; an average current of 20—25 mA was observed. After 5 hr., the sheets were dried at 100° and treated with Cifonelli and Smith's reagents.[3] Subfraction (II) appeared as a single, elongated spot, 8 cm. distant from that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose.

The intrinsic viscosity of subfraction (II) in M-cupriethylenediamine was determined by using a Craig–Henderson viscometer. A value of 0·119 dl./g. was obtained.

Preliminary Examination of Subfraction (III).—The deacetylated material had $[\alpha]_D$ − 20° (*c* 1·0 in 0·1N-NaOH). A portion (55 mg.) was hydrolysed with 2N-sulphuric acid (10 ml.) at 90° for 12 hr. The solution was neutralised with barium carbonate, filtered, de-ionised with Amberlite resin IR-120, and concentrated to a syrup (40 mg.). This was separated into xylose, 4-*O*-methylglucuronic acid, and aldobiuronic acid components on a paper chromatogram

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(30 × 40 cm.) developed in solvent *a* for 2 days with intermediate drying. The relative proportions of the sugars were determined by iodometric titration; a blank chromatogram, developed under identical conditions, was used to correct the results for reducing material extracted from the paper. The ratio of the above components, respectively, was 14·80 : 1·00 : 1·83, corresponding to a ratio of 5·88 : 1·00 for the respective amounts of xylose and 4-*O*-methylglucuronic acid residues in the original polymer.

Preparation of Methylated (II) *and* (III).—Hemicellulose fraction (I) (8·0 g.) was dried thoroughly and then kept in ethereal diazomethane for 7 days. After evaporation of the latter, the material was methylated 8 times with methyl sulphate and aqueous sodium hydroxide (30% w/v) in the usual way. The product (OMe, 32·8%) was dissolved in 5N-sodium hydroxide (500 ml.), and the solution was extracted continuously with chloroform. Evaporation of the extract yielded a residue (2·1 g.), a sample of which gave traces of furfuraldehyde when boiled with 5N-hydrochloric acid (aniline acetate test). After further methylation, first with methyl sulphate and alkali, and then with Purdie's reagents, the residue (1·8 g.; OMe, 38·6%) was dissolved in chloroform (200 ml.) and shaken vigorously with N-sodium carbonate (500 ml.) (3 times). The lower layer was separated, washed with water, dried (Na_2SO_4), and evaporated to yield a residue (1·5 g.) which gave a negative furfuraldehyde test. After remethylation with Purdie's reagents, the product (1·39 g.; OMe, 42·2%) had $[\alpha]_D$ − 10·5° (*c* 2·5 in chloroform). A portion (10 mg.) was demethylated and hydrolysed with hydrobromic acid; [18] chromatography of the products indicated the presence of glucose and mannose, but not of xylose.

The above alkaline solution, after extraction of methylated (II), was acidified with sulphuric acid, and re-extracted continuously with chloroform. Evaporation of the extract gave a residue (4·0 g.), a sample of which gave a strong furfuraldehyde test. After remethylation with Purdie's reagents, the product (3·8 g.; OMe, 38·5%) had $[\alpha]_D$ − 66·8° (*c* 2·1 in acetone). A portion, demethylated and hydrolysed as before, indicated xylose and traces of uronic acids on chromatograms, but no hexoses.

Both methylated products showed slight infrared absorption in the hydroxyl region. They were purified by precipitation from chloroform solution by light petroleum, after which this absorption was negligible.

Examination of Methylated (II).—The material (1·1 g.) was dissolved in 90% w/w formic acid (50 ml.), and water (10 ml.) was added. The solution was heated at 95° {$[\alpha]_D$ −18·0° ⟶ +10° ± 5° (const.; 8 hr.)}. It was then concentrated to yield a syrup; water (20 ml.) was added, and the mixture was heated at 90° (30 min.). The water was then removed, and the product was heated twice more with water in the same way to hydrolyse formyl esters. The yield was 1·0 g. A portion (300 mg.) was separated, on two chromatograms (30 × 40 cm.) developed in solvent *b*, into four fractions (*a*, *b*, *c*, and *d* respectively).

Fraction *a* (8 mg.) travelled on chromatograms developed in solvent *b*, *c*, or *d* at a rate identical with that of 2 : 3 : 4 : 6-tetra-*O*-methyl-D-mannose. Its derived *N*-phenylglycosylamine had $[\alpha]_D$ − 80° (0·5 hr.) ⟶ −8° (const.; 10 hr.) (*c* 0·5 in MeOH), and m. p. 142° undepressed on admixture with 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-mannosylamine. A mixture with the corresponding D-glucosylamine derivative had a melting range 110—115°. An *X*-ray powder photograph of the material was identical with that of the authentic D-mannosylamine derivative.

Fraction b (6 mg.) {$[\alpha]_D$ +59° (*c* 0·4 in EtOH)} was indistinguishable, on chromatograms developed in solvent *b*, *c*, or *d*, from 2 : 3 : 4 : 6-tetra-*O*-methyl-D-galactose. The derived *N*-phenylglycosylamine had m. p. 189°, undepressed on admixture with 2 : 3 : 4 : 6-tetra-*O*-methyl-*N*-phenyl-D-galactosylamine. An *X*-ray powder photograph of the aniline derivative was identical with that of the last-named compound.

Fraction *c* (240 mg.) was inseparable chromatographically in solvents *b* and *c* from the 2 : 3 : 6-tri-*O*-methyl ethers of both D-mannose and D-glucose. In solvent *d* it was partially resolved into spots corresponding to these two sugars. A portion of the mixture (150 mg.) was dissolved in methanol (5 ml.) containing dry hydrogen chloride (1% w/w); the specific rotation of the solution changed as follows:

Time (hr.)	0·0	2·0	12·0	17·0	24·0
$[\alpha]_D^{23}$	+20·3°	+16·6°	0·0°	−1·0°	−0·4°

The solution was neutralised with silver carbonate, filtered and concentrated to a syrup (127 mg.), which was separated on a chromatogram (30 × 40 cm.) with solvent *c*. By spraying

of side-strips, a single reducing component was located and isolated in the usual way. From the area of paper immediately below the reducing component, a second, non-reducing component was isolated.

The reducing component (72 mg.) had $[\alpha]_D$ − 5° (*c* 3·6). When treated with *p*-nitrobenzoyl chloride in pyridine [4] it yielded crystals having $[\alpha]_D$ + 32° ± 1° (*c* 0·5 in chloroform) and m. p. 187—188°, undepressed on admixture with 2 : 3 : 6-tri-*O*-methyl-1 : 4-di-*O*-*p*-nitrobenzoyl-D-mannose (prepared from methylated lucerne seed mannogalactan). The non-reducing component (18 mg.) had $[\alpha]_D$ −4° (*c* 1·0). It was heated in 0·1N-sulphuric acid (5 ml.) at 100° (8 hr.), then the solution was neutralised with barium carbonate, filtered, and concentrated to a syrup (12 mg.), which was treated with *p*-nitrobenzoyl chloride and pyridine as above. The product had $[\alpha]_D$ −33° ± 1° (*c* 0·5 in chloroform) and m. p. 186°, undepressed on admixture with 1 : 4-di-*O*-*p*-nitrobenzoyl-2 : 3 : 6-tri-*O*-methyl-D-glucose (prepared from methylated amylopectin).

Fraction *d* (10 mg.) had $[\alpha]_D$ +20° ± 3° (*c* 0·6 in acetone). On chromatograms developed in solvent *d* for 24 hr. with intermediate drying, it travelled as three spots; the major component was chromatographically indistinguishable from 2 : 3-di-*O*-methyl-D-mannose. Demethylation of *d* with hydrobromic acid [19] gave a product travelling as mannose on chromatograms developed in solvents *b* and *c*.

Examination of Methylated (III).—The osmotic pressures of four different concentrations of the material in chloroform–ethanol (90 : 10 v/v) were determined, with a Zimm–Myerson–Stabin–Immergut osmometer. A number-average molecular weight of 13,550 ± 400 was indicated.

The methylated material (0·80 g.) was dissolved in 90% w/w formic acid, (25 ml.) and water (25 ml.) was added. The clear solution was heated at 90°; the specific rotation changed as follows:

Time (hr.)	0·00	0·33	0·67	1·00	2·00	3·00	4·50
$[\alpha]_D^{25}$	−56·8°	−26·3°	0·00°	+13·1°	+29·4°	+33·0°	+34·4°

The hydrolysate was concentrated to a syrup, which was heated with water as before to hydrolyse formyl esters. The product (0·75 g.) travelled, on chromatograms developed in solvents *a* and *c*, as three neutral spots (*a'*, *b'*, and *c'* respectively) and two acidic spots (*d'* and *e'* respectively). In solvent *d*, *d'* and *e'* travelled slowly as elongated yet separate spots. A portion (600 mg.) was separated on four chromatograms (30 × 40 cm.) with solvent *d*. A part of one chromatogram (10 × 40 cm.) was used to estimate the relative amounts of the five components by iodometric titration. A blank chromatogram was used to correct the results in the usual way. The ratio *a'* : *b'* : *c'* : *d'* : *e'* was 3·2 : 59·4 : 2·9 : 1·0 : 9·9.

Component a' (12 mg.) had $[\alpha]_D$ +18° (*c*. 2·4); it was indistinguishable on chromatograms developed in solvent *b*, *c*, or *d* from 2 : 3 : 4-tri-*O*-methyl-D-xylose, and crystallised in part on being seeded with this compound. The derived *N*-phenylglycosylamine had $[\alpha]_D$ −80° ± 5° (5 min.) ⟶ +40° ± 5° (24 hr.) (*c*, 0·8 in MeOH), and m. p. 100—102°, undepressed on admixture with 2 : 3 : 4-tri-*O*-methyl-*N*-phenyl-D-xylosylamine.

Component *b'* (350 mg.) was chromatographically indistinguishable (solvent *b*, *c*, or *d*) from 2 : 3-di-*O*-methyl-D-xylose, and completely crystallised on being seeded with this compound. The crystals had $[\alpha]_D$ +65° (5 min.) ⟶ +23° (12 hr.) (*c*, 2·0), m. p. and mixed m. p. 80°. The derived *N*-phenylglycosylamine had m. p. 126°

Component *c'* (15 mg.) had $[\alpha]_D$ +19° (*c* 3·0), and travelled on chromatograms (solvent *b*, *c*, or *d*) at a rate identical with that of both 2-*O*- and 3-*O*-methyl-D-xylose. On paper electrophoretograms, at least 90% of the material travelled at the same rate as 3-*O*-methyl-D-xylose, the remainder travelling as the 2-*O*-isomer. A further quantity of methylated subfraction (III) (1·5 g.) was hydrolysed as before, and the hydrolysate was passed, in aqueous solution, through a column (2 × 20 cm.) of Amberlite resin IR-45 (acetate form). Concentration of the effluent and washings yielded a syrup (1·1 g.) which was adsorbed on a column (2 × 20 cm.) of cocoa-bean shell charcoal.[20] Elution with aqueous ethanol (4% v/v; 1 l.) afforded an electrophoretically pure fraction (30 mg.) which crystallised when seeded with 3-*O*-methyl-D-xylose. The crystals had m. p. and mixed m. p. 96—98°.

Component *d'* (5 mg.) had $[\alpha]_D$ +45° ± 5° (*c* 1·0), and travelled on chromatograms developed in solvent *a* at a rate similar to that reported for 2 : 3 : 4-tri-*O*-methyl-D-glucuronic acid.

[20] Barth and Timell, *Canad. J. Chem.*, 1958, **36**, 1321.

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Component *e'* (56 mg.) had $[\alpha]_D$ +49° (*c* 0·4) (Found: OMe, 32·1%; equiv., 374. Calc. for $C_{15}H_{26}O_{11}$: OMe, 32·5%; equiv., 382). The column of Amberlite resin IR-45 (above) was eluted with aqueous 10% v/v formic acid (300 ml.). Concentration of the effluent yielded a syrup (168 mg.), which was combined with the components *d'* and *e'* previously isolated, and then boiled with methanolic 2% w/w hydrogen chloride (50 ml.) for 6 hr. The solution was neutralised with silver carbonate, filtered, and concentrated to give a syrup; this was dissolved in ether (50 ml.) and reduced with lithium aluminium hydride (200 mg.). The product (135 mg.) was isolated in the usual way. A portion (60 mg.) was hydrolysed with aqueous 20% v/v formic acid (10 ml.) at 90° for 8 hr. Formyl esters were then hydrolysed as before, and the products were resolved on a chromatogram (30 × 40 cm.) (solvent *d*) into (i) 2 : 3 : 4-tri-*O*-methyl-D-glucose, identified by conversion into its *N*-phenylglycosylamine, $[\alpha]_D$ −125° ± 5° (5 min.) (*c* 0·54 in MeOH), m. p. 144—146°, and (ii) 3-*O*-methyl-D-xylose, tentatively identified by its electrophoretic mobility and its infrared absorption spectrum, $[\alpha]_D$ +18° (*c* 1·2).

A further portion of the reduced disaccharide was methylated with Purdie's reagents; the product (55 mg.) had $[\alpha]_D$ +104° (*c* 1·1 in chloroform) and showed negligible infrared absorption in the hydroxyl region. It was hydrolysed as before, and the products were separated into (iii) 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, identified by conversion into the corresponding *N*-phenylglucosylamine, $[\alpha]_D$ +240° (*c* 0·6 in acetone), m. p. and mixed m. p. 138°, and (iv) 3 : 4-di-*O*-methyl-D-xylose, identified by conversion into 3 : 4-di-*O*-methyl-D-xylonolactone, $[\alpha]_D$ −50° ⟶ −23° (3 days; *c* 1·1), m. p. and mixed m. p. 64—65°.

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118. *Heats of Combustion and Molecular Structure. Part VII.*[1] 1 : 3-*Dioxa-* *and* 1 : 3 : 5-*Trioxa*-cycloalkanes.

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The heats of combustion and latent heats of evaporation of three cyclic ethers, containing the 1 : 3-dioxa-grouping, have been measured. The derived atomic heats of formation have been analysed into mean bond-energy terms. The results indicate that this grouping stabilises the molecules.

IN previous Parts the mean bond-energy term for the C–O bond in ethers has been determined [2] and the thermochemistry and structures of some cyclic ethers considered.[1,2] It was during these investigations that the heat of combustion of paraldehyde was reported.[3] It appears that the paraldehyde molecule is more stable than would be expected from the sum of the mean bond-energy terms of the component bonds. This unexpected stabilisation energy is also apparent from data on heats of combustion, although to a smaller extent, in *sym*-trioxan [4] and in the acetals.[5,6]

Elucidation of the problem has been approached by considering the energetics of some di-ethers, with oxygen atoms in both the 1 : 3- and the 1 : 4-positions. The heats of combustion and latent heats of evaporation of 1 : 3-dioxan (I), 5 : 5'-*spiro*bis-1 : 3-dioxan

[1] Part VI, Cass, Fletcher, Mortimer, Quincey, and Springall, *J.*, 1958, 2595.
[2] Cass, Fletcher, Mortimer, Springall, and White, *J.*, 1958, 1406.
[3] Cass, Springall, and White, *Chem. and Ind.*, 1955, 387.
[4] Walker and Carlisle, *Chem. Eng. News*, 1943, **21**, 1251.
[5] Kharasch, *J. Res. Nat. Bur. Stand.*, 1929, **2**, 359.
[6] Wheland, "Resonance in Organic Chemistry," Wiley, New York, 1955, pp. 89, 95.

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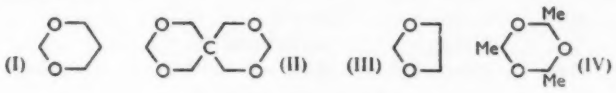
(II) and 1 : 3-dioxolan (III) have been measured. Experimental data on paraldehyde (IV) are also recorded.



Experimental

Preparation of Materials.—" B.D.H. Thermochemical Standard " benzoic acid was used.

5 : 5′-*spiro*Bis-1 : 3-dioxan was prepared by Read's method,[7] and after three crystallisations from ether had m. p. 50·0°, as given by Read.

1 : 3-Dioxan was prepared from trimethylene glycol and methylene sulphate according to Baker's method.[8] It was refluxed over sodium and fractionated; the product had b. p. 104·0—104·5°/746 mm. (Baker gives b. p. 105°/754 mm.).

1 : 3-Dioxolan, prepared from ethylene glycol and methylene sulphate,[8] was refluxed over sodium and fractionated, the fraction collected having b. p. 74·0°/738 mm. (Baker gives b. p. 76°/752 mm.).

Paraldehyde, B.D.H. reagent quality, was dried ($CaCl_2$) and fractionated through an 8 in. column packed with glass helices. The fraction of b. p. 124·5°/767 mm. was collected (Timmermans [9] gives b. p. 124·35°/760 mm.).

Vapour-pressure Measurements.—The vapour pressures of the compounds were measured in an apparatus of the type described by Sanderson.[10] The values A and B of the equation $\log_{10} p(\text{mm.}) = -A/T + B$ are given in Table 1. The derived latent heats of vaporisation

Table 1.

Compound	A	B	L_v (kcal./mole)
5 : 5′-*spiro*Bis-1 : 3-dioxan	2942	7·79	13·4 ± 0·4
1 : 3-Dioxan	1869	6·78	8·5 ± 0·2
1 : 3-Dioxolan	1854	7·21	8·5 ± 0·1
Paraldehyde	2168	7·34	9·9 ± 0·1

(liquid to vapour), given by $L_v = 4{\cdot}57A \times 10^{-3}$ kcal./mole, are also listed. The latent heat of sublimation of 5 : 5′-*spiro*bis-1 : 3-dioxan is assumed to be 4·0 kcal./mole greater than its latent heat of vaporisation.

Combustion Calorimetry.—The combustions of 5 : 5′-*spiro*bis-1 : 3-dioxan, 1 : 3-dioxan, and 1 : 3-dioxolan were made in the twin-valve bomb (The Parr Instrument Co., Moline, Illinois, U.S.A.) described in Part IV.[11] Temperature changes were recorded by a platinum resistance thermometer and the energy equivalent, E, of the calorimeter was determined by burning benzoic acid pellets. The products of combustion were analysed for carbon dioxide [12] with an accuracy of ±0·05% and in most cases the weight of carbon dioxide was less than that calculated for complete combustion by amounts varying from 0·3 to 0·6%. In no case was carbon found in the bomb after combustion and it was assumed that the discrepancy was due to unburnt ether or traces of water. The results are recorded in Table 2.

After the combustion of 5 : 5′-*spiro*bis-1 : 3-dioxan the calorimeter system was modified as follows. The original solid Baekelite lid to the calorimeter jacket, carrying a reciprocating stirrer, was replaced by a hollow copper lid, through which passes the circulating water, at 28·000 ± 0·005° c, from the calorimeter jacket. This new copper lid carries two counter-rotating propeller stirrers made of twisted brass sheet.

Paraldehyde was burnt in a Mahler–Cook stainless-steel bomb, temperature changes being recorded by a Beckmann thermometer, according to the procedure described in Part I.[13] The energy equivalent of the calorimeter system, E', was $308{\cdot}5 + 24{\cdot}18\theta_m$ cal./deg., where θ_m is a mean temperature as defined in Part I. Combustions were made on three different specimens

[7] Read, *J.*, 1912, **101**, 2093.
[8] Baker, *J.*, 1931, 1765.
[9] Timmermans, " Physico-chemical Constants of Pure Organic Compounds," Elsevier, Brussels, 1950.
[10] Sanderson, " Vacuum Manipulation of Volatile Compounds," Wiley, New York, 1948, p. 48.
[11] Cass, Fletcher, Mortimer, Quincey, and Springall, *J.*, 1958, 958.
[12] Prosen and Rossini, *J. Res. Nat. Bur. Stand.*, 1941, **27**, 289.
[13] Springall, White, and Cass, *Trans. Faraday Soc.*, 1954, **50**, 815.

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independently by Drs. T. R. White and R. C. Cass.[3] The results were closely concordant. Data for one specimen are recorded (Table 3).

TABLE 2.

Wt. taken,* m (g.)	ΔR (ohm)	CO_2 (obs. : calc.)	Corrections (cal.) † (fuse)	(HNO_3)	C (cal./ohm	$-\Delta U_b$ ‡ (kcal./mole)
		5 : 5′-spiro*Bis*-1 : 3-*dioxan* (M, 160·17)				
0·6524	0·08998	0·9780	6·0	0·8	4·8	901·4
0·7116	0·09994	0·9978	6·0	0·8	5·3	899·8
0·8174	0·11475	0·9937	6·0	1·4	6·1	903·2
0·9154	0·12824	0·9969	6·0	3·5	6·8	898·2
0·9533	0·13379	0·9977	6·0	2·9	7·0	899·3
		E = 39980 ± 10 cal./ohm				
		1 : 3-*Dioxan* (M, 88·10)				
0·4589	0·07448	0·9970	18·4	1·0	4·0	556·4
0·3720	0·05888	0·9747	20·0	0·7	3·2	553·7
0·4212	0·06858	0·9981	21·1	0·8	3·6	554·6
0·3831	0·06247	0·9975	10·4	0·8	3·3	554·6
		E = 39058 ± 10 cal./ohm				
		1 : 3-*Dioxolan* (M, 74·05)				
0·4724	0·06664	0·9995	14·8	0·6	3·7	405·6
0·4781	0·06813	0·9994	22·5	1·3	3·7	408·3
0·6238	0·08836	0·9995	23·2	2·1	4·8	406·5
0·3923	0·05366	0·9997	28·6	1·3	3·0	404·8
		E = 39058 ± 10 cal./ohm				

* Weight *in vacuo*.

† Made necessary by heat effects due to the combustion of the fuse and the oxidation of nitrogen.

‡ Where $-\Delta U_b = 10^{-3}M/m'[(E + C)\Delta R$ — Corr. (fuse + HNO_3)] kcal./mole and $m' = m_{(vac.)} \times CO_2$ (obs. : calc.).

TABLE 3.

Wt. taken,* m (g.)	$\Delta\theta$ (°)	θ_m (°)	Corrections (cal.).† (fuse)	(HNO_3)	(carbon)	E' (cal./deg.)	C (cal./deg.)	$-\Delta U_b$ ‡ (kcal./mole)
			Paraldehyde (M, 132·16)					
1·2094	2·3453	4·210	71·8	3·8	2·3	3187·0	1·0	809·0
1·1663	2·2616	4·403	71·8	4·2	0·8	3192·0	1·0	809·8
1·1834	2·2944	4·406	71·8	3·8	0·8	3192·0	1·0	809·8

* Weight *in vacuo*.

† Made necessary by heat effects due to the combustion of the fuse, the oxidation of nitrogen, and deposition of some free carbon.

‡ Where $-\Delta U_b = 10^{-3}M/m[(E' + C)\Delta\theta$ — corr. (fuse + HNO_3 — carbon)] kcal./mole.

The $-\Delta U_b$ terms were converted into $-\Delta H_c°$ terms, the standard heat of combustion, by using the expression

$$-\Delta H_c° = -\Delta U_b - w - \Delta nRT$$

where w is the Washburn correction, calculated according to Prosen,[14] and Δn is the number of moles of gas produced in the combustion reaction. The results are recorded in Table 4.

TABLE 4.

Compound	$-\Delta U_b$ mean (kcal./mole)	Standard deviation ($-\Delta U_b$) (%)	Overall uncertainty interval (%)	Washburn corr. w (kcal./mole)	ΔnRT (kcal./mole)	$-\Delta H_c°$ (kcal./mole)
5 : 5′-*spiro*Bis-1 : 3-dioxan	900·4	±0·10	±0·14	0·6	−0·6	900·4
1 : 3-Dioxan	554·8	±0·23	±0·25	0·4	−0·6	555·0 *
1 : 3-Dioxolan	406·3	±0·20	±0·22	0·2	−0·3	406·4 *
Paraldehyde	809·5	±0·033	±0·042	0·4	−0·9	810·0

* Skuratov [15] has recently recorded slightly higher values of $-\Delta H_c°$ for these compounds (557·4 and 407·6 kcal./mole, respectively).

[14] Prosen, "Experimental Thermochemistry," ed. Rossini, Interscience, New York, 1956.

[15] Skuratov, Kozina, Shteher, and Varushyenko, "IUPAC Thermochemical Bulletin," 1957, **3**.

Discussion

The $-\Delta H_f°$ terms for the compounds were calculated from $-\Delta H_c°$ terms by using the values $\Delta H_f°$ for water = −68·32 and $\Delta H_f°$ for carbon dioxide = −94·05 kcal./mole.[16] By incorporating the L_v terms, the heats of atomisation, ΔH_a, C, 171·1,[17] H, 52·09,[16] and O, 58·98 kcal./g.-atom,[18] and atomic heats of formation, $-\Delta H_{f,g}^a$, were derived. From the values [2] $\bar{E}$(C–C) 83·1, $\bar{E}$(C–H) 98·85, and $\bar{E}$(C–O) 84·3 kcal./mole a summation was made of mean bond-energy terms in the molecule, $\sum\bar{E}$(b), and the difference, $-\Delta H_{f,g}^a - \sum\bar{E}(b) = E_s$, the stabilisation energy, was evaluated. Similar evaluations of E_s terms have been made from published $-\Delta H_c°$ data for 4-methyl-1 : 3-dioxan (709·8; [15] assuming $L_v = 9$), *sym*-trioxan (356·7; [4] $L_v = 9·6$ [4]), 1 : 4-dioxan (554·6; [19] $L_v = 8·5$ [9]), and 1 : 2-diethoxyethane (924·6; [6] assuming $L_v = 10$) [all data in kcal./mole]. These data are given in Table 5.

Table 5.

Compound	Enthalpy terms $-\Delta H_{f,g}^a$	$\sum\bar{E}$(b)	E_s (kcal./mole)	Compound	Enthalpy terms $-\Delta H_{f,g}^a$	$\sum\bar{E}$(b)	E_s (kcal./mole)
1 : 3-Dioxan	1307·4	1294·2	13·2	Paraldehyde	1731·8	1688·4	43·4
4-Methyl-1 : 3-dioxan	1600·4	1585·0	15·4	1 : 4-Dioxan	1307·2	1294·2	13·0
5 : 5′-*spiro*Bis-1 : 3-dioxan	2213·3	2193·0	20·3	1 : 2-Diethoxyethane	1984·4	1970·4	14·0
sym-1 : 3 : 5-Trioxan ...	870·8	846·0	24·8	1 : 3-Dioxolan	1017·8	1013·4	4·4

1 : 3-Dioxan has E_s = 13·2 kcal./mole. It is likely that the molecule is free from strain due to distortion of bond angles, as is that of 1 : 4-dioxan.[20] For 4-methyl-1 : 3-dioxan, the E_s term, 15·4 kcal./mole, is 2·2 kcal./mole greater than for 1 : 3-dioxan. This difference is similar to that between similar terms for *cyclo*hexane and methyl*cyclo*hexane, 2·6 kcal./mole,[21] so that the stabilisation energy due to the 1 : 3-dioxa-group in both compounds is 13 kcal./mole. With 5 : 5′-*spiro*bis-1 : 3-dioxan the E_s value, 20·3 kcal./mole, is somewhat less than twice this value.

This type of stabilisation has already been reported [3] in six-membered cyclic 1 : 3 : 5-trioxa-compounds, *sym*-trioxan (24·8 kcal./mole) and paraldehyde (43·4 kcal./mole). A similar, rather smaller effect is found in open-chain 1 : 3-dioxa-compounds, *i.e.*, the acetals, formaldehyde dimethyl acetal, formaldehyde diethyl acetal, and acetaldehyde dimethyl acetal which all show stabilisation energies of 7 kcal./mole.[6]

This additional stability is also found in molecules containing two oxygen atoms in the 1 : 4-position (*e.g.*, 1 : 4-dioxan, E_s = 13 kcal./mole; 1 : 2-diethoxyethane, E_s = 14 kcal./mole).

The stabilisation energy, E_s, of 1 : 3-dioxolan is 4·4 kcal./mole, whereas *cyclo*pentane has a " strain " energy of 6 kcal./mole (E_s = −6 kcal./mole).[22] It is probable that the molecules of both these compounds are free from strain due to distortion of bond angles, the strain observed in *cyclo*pentane being due mainly to repulsive forces between hydrogen atoms bonded to adjacent carbon atoms.[23] [With tetrahydrofuran the strain is reduced [2] to 3 kcal./mole (E_s = −3 kcal./mole).]

These C–O bonds have [20] the length (1·42 ± 0·03 Å) of normal C–O single bonds.[24] It seems likely that the cause of the stabilisation of the di- and tri-oxa-compounds, relative to the corresponding saturated hydrocarbons, is reduction in the repulsive forces between non-bonded hydrogen atoms, arising from the replacement of the $\cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot$ systems

[16] National Bureau of Standards Circular 500, Washington, 1952.
[17] Brewer and Kane, *J. Phys. Chem.*, 1955, **59**, 105.
[18] Brix and Herzberg, *J. Chem. Phys.*, 1953, **22**, 2240.
[19] Roth and Meyer, *Z. Elektrochem.*, 1933, **39**, 35.
[20] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.
[21] Selected Values of Properties of Hydrocarbons, American Petroleum Institute, Research Project 44, 1954.
[22] Dolliver, Gresham, Kistiakowsky, and Vaughan, *J. Amer. Chem. Soc.*, 1937, **59**, 831.
[23] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, N.Y., 1940, p. 91.
[24] *Idem, op. cit.*, p. 167.

by $\cdot CH_2 \cdot O \cdot CH_2$ systems. Even so the high degree of stabilisation shown by paraldehyde and the low degree shown by the open-chain acetals seem anomalous.

It is probably not legitimate to press the analysis further because, as Sidgwick [25] and others (*e.g.*, Dewar [26]) have pointed out, for a rigorous intramolecular structural analysis, enthalpy terms should be measured at, or corrected to, 0° K (ΔH_0 terms). For a given change in a particular molecular system, the thermochemically measured $\Delta H'_{298}$ term is related to the corresponding $\Delta H'_0$ term by the Kirchhoff expression

$$\Delta H'_{298} = \Delta H'_0 + \int_0^{298} \Delta C'_p dT,$$

where $\Delta C'_p$ is the change in the specific heat of the system during the reaction at a particular temperature. The $\Delta C'_p$ integral term, which accounts for the kinetic component of $\Delta H'_{298}$ not included in the zero-point energy, is usually unknown but is normally small relative to $\Delta H'_0$.

When considering the difference between this $\Delta H'_{298}$ and the $\Delta H''_{298}$ for the corresponding change in another system (the standard procedure in thermochemical studies on molecular structure), we have

$$\Delta H'_{298} - \Delta H''_{298} = \Delta H'_0 - \Delta H''_0 + \int_0^{298} (\Delta C'_p - \Delta C''_p) dT$$

Provided $\Delta H'_{298} - \Delta H''_{298}$ is large it may reasonably be taken as a measure of $\Delta H'_0 - \Delta H''_0$ and we may neglect the heat component due to the ΔC_p integrals. When, however, $\Delta H'_{298} - \Delta H''_{298}$ is small, it cannot safely be taken as a measure of $\Delta H'_0 - \Delta H''_0$ because the term due to the ΔC_p integrals may be of comparable magnitude. As Dewar [26] has pointed out, there is no reason why this integral term should be susceptible to analysis into constant bond components, and there are grounds for expecting that in formation reactions it will be larger for an open-chain compound than for a ring analogue.

We are indebted to Imperial Chemical Industries Limited for a grant.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE, KEELE. [*Received, June 30th,* 1958.]

[25] Sidgwick, " The Covalent Link in Chemistry," Cornell Univ. Press, Ithaca, N.Y., 1933, p. 101.
[26] Dewar, *Trans. Faraday Soc.*, 1946, **42**, 767.

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119. *Ribose and its Derivatives. Part VIII.* The Ring Structure and Periodate Oxidation of Ribose and Related Polyols.*

By G. R. BARKER and D. F. SHAW.

A study has been made of the course of the reaction between the periodate ion and *cis-cis*-1 : 2 : 3-triols in which the hydroxyl residues are attached to a six-membered ring. It is concluded that, at the moment of dissolution in water, ribose exists in the pyranose form. The stereochemical requirements for the reaction, including the effect of conformation, are discussed. A new method is put forward for the assessment of relative stabilities of " chair " conformations of pyranose rings.

ALL natural derivatives of ribose possess the furanose structure. On the other hand, the cyclic form adopted by the free sugar is still in some doubt, since its rapid complex mutarotation probably involves more than one ring form.[1] It has been stated [2] that crystalline D-ribose exists in the pyranose form on the grounds that benzoylation at low

* Part VII, *J.*, 1956, 2656. Part of the present work was reported by Barker and Shaw, *Proc. Chem. Soc.*, 1957, 259.

[1] Phelps, Isbell, and Pigman, *J. Amer. Chem. Soc.*, 1934, **56**, 747.
[2] Ness, Diehl, and Fletcher, *ibid.*, 1954, **76**, 763.

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temperature in presence of pyridine yields a 1 : 2 : 3 : 4-tetrabenzoate. Even under these conditions, however, interchange between the various possible structures is likely to be rapid. We have studied the ring structure of ribose by periodate oxidation, which we believe to be, under certain conditions, more rapid than the reactions associated with mutarotation.

It has been shown [3] that a number of reducing sugars are oxidised by sodium metaperiodate in their lactol forms, and 2-*O*-formylglyceraldehyde has been isolated after periodate oxidation of D-glucose in unbuffered solution.[4] By analogy, it was envisaged that oxidation of ribose might result in initial, rapid consumption of 2 mols. of oxidant if a furanose ring were present, or of 3 mols. if a pyranose ring were concerned. However, in unbuffered solution, 4 mols. of periodate were rapidly consumed, with no discontinuity in the rate of uptake. In presence of phosphate buffer at pH 7·0, determination of periodate by the arsenite method [5] showed the immediate disappearance of approximately 1 mol. of oxidant, with a subsequent slow further uptake. Similar results were obtained on using a phthalate buffer at pH 6·2, the secondary uptake being somewhat faster in this case. It is clear that, in the presence of these buffers, the reaction proceeds by neither of the schemes mentioned above. It may also be concluded that the behaviour is not due to combination of the phosphate and periodate ions.[6] Also, the results cannot be explained by an association of the phosphate ion with ribose, since its specific rotation after mutarotation in phosphate buffer is the same as at equilibrium in aqueous solution. Similar phases in the uptake of periodate were observed between pH 6·2 and 8·0; below pH 6·0 more than 1 mol. of oxidant was rapidly consumed.

In order to determine the nature of the reaction taking place under the conditions described above, crystalline ribose was added to one molar equivalent of sodium metaperiodate in phosphate buffer at pH·7·0, and the resulting solution was chromatographed on paper. A strong spot corresponding to ribose was obtained, and it was estimated by Baar's method [7] that approximately 60% of the original ribose was recovered. To explain this, we suggest that, under the conditions described, ribose and the periodate ion combine in equimolecular proportions to form a complex which can decompose either to give ribose and periodate again, or to give oxidation products and iodate:

$$\text{Ribose} + IO_4^- \underset{}{\overset{\text{Fast}}{\rightleftharpoons}} \text{Complex} \xrightarrow{\text{Slow}} \text{First oxidation product}$$

$$\text{Complex} \xrightarrow[\text{Fast}]{IO_4^-} CH_2O + H{\cdot}CO_2H$$

Under the conditions of the experiment, the position of equilibrium appears to lie far over to the right. In agreement with this, it was found that, with aliquot parts taken early in an experiment, the faint colour of iodine obtained at the end-point of the titration slowly increased in intensity, presumably owing to the liberation of periodate ions by decomposition of the complex. This " drift " in the end-point was not observed with later portions in which much of the complex had decomposed. The reversible nature of the initial reaction was also shown by the fact that if, after treatment of ribose with periodate at pH 7, the solution is acidified and the periodate determined with potassium iodide and sodium thiosulphate, the apparent uptake of periodate is smaller than when the titration is done in alkaline solution. The concentration of the complex at time t is proportional to the difference between the final consumption of periodate and the apparent uptake after time t. A plot of the logarithm of this difference against time indicates that, up to a point at which 75% of the ribose has been oxidised, decomposition of the complex follows a first-order equation, in accordance with the proposed scheme of reactions.

[3] Barker and Smith, *Chem. and Ind.*, 1952, 1035, and references therein.
[4] Schöpf and Wild, *Chem. Ber.*, 1954, **87**, 1571.
[5] Hughes and Nevell, *Trans. Faraday Soc.*, 1948, **44**, 941.
[6] Bell, Palmer, and Johns, *J.*, 1949, 1536.
[7] Baar, *Biochem. J.*, 1954, **58**, 175.

Isolation of the complex proved impossible owing to its progressive decomposition. In order to determine the nature of the complex, the behaviours of other polyols of known structure were studied. Buist and Bunton [8] have shown by kinetic measurements that an intermediate complex is formed at pH 4·5 between periodate and 2-methylbutane-2 : 3-diol but it will appear from the following discussion that the complex now postulated is of a different type.

In Table 3 are given the rates of uptake of periodate by a variety of polyols. In buffered solution, most hexose and pentose sugars were found to consume three or more mols. of oxidant very rapidly. Exceptions are D-ribose, D-lyxose, D-gulose, D-talose, and D-allose (compare, in Table 3, nos. 7, 8, 16, 17, and 18 with nos. 9, 10, 11, 12, 13, 14, and 15). The same distinction exists between *cis-trans-cyclo*hexane-1 : 2 : 3-triol and *cis-cis-cyclo*hexane-1 : 2 : 3-triol (nos. 20 and 21). Most pyranosides behave differently from the parent sugars in exhibiting a slow and steady uptake of periodate. Benzyl and methyl β-D-ribopyranoside are exceptional in that, like the parent sugar, they immediately consume approximately 1 mol. The subsequent uptake is even slower than in the case of the parent sugar. From these results it is seen that the immediate consumption of 1 mol. of periodate followed by a slow further uptake (the rate in this second phase varies from one case to another) is characteristic of compounds possessing a *cis-cis*-1 : 2 : 3-triol system in a six-membered ring, as an obligatory or a potential element of their structure. We attribute this anomalous behaviour to complex formation as described above for ribose and the results are summarised in Table 1 (column *A*). This behaviour is not observed with ribitol, 5-*O*-triphenylmethyl-D-ribose, or 5-*O*-methyl-D-ribose (Table 3, nos. 19, 37, 38), thus excluding acyclic or five-membered ring systems. The rates of uptake of periodate by diols cannot be analysed in the same way, but in no case was any increase in the colour of iodine observed at the end-point of the titration and we do not believe that diols undergo reversible complex formation. Furthermore, *trans-trans-cyclo*hexane-1 : 3 : 5-triol, which forms complexes with the cuprammonium ion,[9] does not interact with the periodate ion under these conditions.

It may be mentioned that Christian, Gogek, and Purves [10] observed that in the periodate oxidation of *cyclo*hexanetriols the rate of uptake of the first mol. of oxidant is very much higher by the totally *cis*-isomer than by the others, but they did not measure the rate of consumption of periodate beyond this point.

The Structure of Ribose.—From the above discussion, formation of the type of complex now described appears to be diagnostic for a *cis-cis*-triol system in a six-membered ring, from which it follows that, at the moment of dissolution, D-ribose exists in the pyranose form. The same may be said of D-lyxose, and, since the requirements for complex formation are fulfilled only in the β-structure, it is concluded that the crystalline sugar is β-D-lyxopyranose. It is interesting that, after mutarotation, D-lyxose gives no evidence of complex formation. In contrast, no distinction can be made between α- and β-D-ribopyranose on the basis of periodate oxidation, because the 1-, 2-, and 3-hydroxyl groups or those at positions 2, 3, and 4 may be involved in complex formation. However, if solutions of ribose are allowed to mutarotate for varying intervals of time, the initial uptake of periodate progressively increases to a new constant value. This is thought to imply that, during the mutarotation, structures other than α- or β-D-ribopyranose are formed. It is calculated that, at equilibrium, approximately 20% of the sugar is in a form which does not form complexes. This is in agreement with Phelps, Isbell, and Pigman's view [1] that the initial reaction during the mutarotation of ribose involves a change in the size of the ring. Cantor and Peniston [11] have deduced from polarographic measurements that, after mutarotation, solutions of ribose contain 8·5—30% of a form

[8] Buist and Bunton, *J.*, 1957, 4580.
[9] Reeves, *J. Amer. Chem. Soc.*, 1949, **71**, 2116.
[10] Christian, Gogek, and Purves, *Canad. J. Chem.*, 1951, **29**, 911.
[11] Cantor and Peniston, *J. Amer. Chem. Soc.*, 1940, **62**, 2113.

TABLE 1.

Compound	*A* Complex formation with periodate	*B* Total overlap (Å) (1C–C1)	*C* Anhydride (%)
β-D-Glucose ...		1·82	2
β-D-Galactose ...		1·70	Small
β-D-Mannose ...	−	1·65	Small
β-D-Talose	+	1·53	Small
β-D-Allose	+	1·30	14
β-D-Gulose † ...	+	1·18	43
β-D-Altrose	−	1·13	57
β-D-Idose *	−	1·01	75
α-D-Glucose ...	−	0·98	
α-D-Galactose ...	−	0·85	
α-D-Mannose ...		0·80	
β-D-Xylose		0·71	
α-D-Talose		0·68	
β-D-Lyxose	+	0·54	
α-D-Allose		0·45	
β-D-Ribose	+	0·40	

Compound	*A* Complex formation with periodate	*C* Total overlap (Å) (1C–C1)
α-D-Gulose		0·33
α-D-Altrose		0·28
β-D-Arabinose	−	0·23
α-D-Idose *	−	0·16
α-D-Xylose	−	0·06
α-D-Lyxose		−0·23
α-D-Ribose		−0·37
α-D-Arabinose		−0·54
*cis-cis-cyclo*Hexane-1 : 2 : 3-triol	+	0·43
CH_2Ph β-D-ribopyranoside	+	0·40
Me β-D-ribopyranoside ...	+	0·40
Me β-D-xylopyranoside.....	−	0·71
Me α-D-lyxopyranoside.....	−	−0·23
Me α-D-glucopyranoside ...	−	0·98
CH_2Ph β-D-glucopyranoside	−	1·82

Compound	*A* Complex formation with periodate
Lævoglucosan	−
1 : 6-Anhydro-D-allopyranose...	+
Benzyl β-D-ribofuranoside	−
5-*O*-Triphenylmethyl-D-ribose	−
5-*O*-Methyl-D-ribose	−
Ribitol	−

Compound	*A* Complex formation with periodate
*cis-cyclo*Pentane-1 : 2-diol	−
*trans-cyclo*Pentane-1 : 2-diol	−
*cis-cyclo*Hexane-1 : 2-diol	−
*trans-cyclo*Hexane-1 : 2-diol	−
*cis-cis-trans-cyclo*Hexane-1 : 2 : 3-triol	−
*trans-trans-cyclo*Hexane-1 : 3 : 5-triol	−

* The syrupy anomeric mixture was used. † The crystalline calcium chloride compound was used.

which is more rapidly reduced than the rest. We cannot conclude from our results anything concerning the nature of the structures produced during the mutarotation of ribose, since neither an acyclic nor a furanose form would be expected to give a stable complex with periodate. We emphasise, however, that since the initial reaction is not an anomerisation, it is not permissible to conclude from the direction of the initial change of rotation that crystalline ribose is β-D-ribopyranose. Only the size of the ring can be regarded as established.

The Nature of the Complex and the Behaviour of Mannose.—It has been suggested [12] that the rate-determining step in the fission of glycols by periodate is the formation of a cyclic diester of periodic acid. On the assumption that the complexes formed between the periodate ion and triols are triesters, it appeared that the size of the periodate ion might be a critical factor in determining the stability of the complex. We therefore investigated the possibility of reaction between triols and the tellurate ion, since this ion approximates closely in size to that of the periodate ion. The possibility also existed of isolating a complex with telluric acid since there would be no tendency toward oxidative decomposition. It was first ascertained that, in the absence of buffer at pH 8, the formation of a complex between a triol and periodate was accompanied by a sharp drop in pH, followed by a slow increase, whereas with those triols which do not form complexes, a slow but small increase in pH is observed. The pH of a solution of telluric acid, previously adjusted to pH 8·0 with sodium hydroxide, fell after the addition of ribose or other compounds which form complexes with periodate, whereas no change in pH was observed with compounds which do not form complexes. This is taken to indicate that the tellurate ion forms complexes analogous to those with the periodate ion. In this case, however, complex formation took place much more slowly and it was not possible to isolate the

[12] Price and Knell, *J. Amer. Chem. Soc.*, 1942, **64**, 552, and references therein.

complex. Further evidence for complex formation with tellurate is that the initial uptake of periodate by *cis-cis-cyclo*hexane-1 : 2 : 3-triol is considerably reduced by prior addition of tellurate. No such effect was obtained in the oxidation of the *cis-cis-trans*-isomer. The analogous behaviour of the two ions of similar size confirmed our view that the formation of complexes with triols depends on specific stereochemical factors and we therefore next considered the conformations of triols which undergo this reaction.

It is reasonable to assume that, in order to form a complex with periodic acid, a cyclic *cis-cis*-1 : 2 : 3-triol adopts the conformation in which two hydroxyl groups occupy axial positions and one an equatorial position. However, this is not the preferred conformation in many cases, and it is concluded that a compound may take up an unfavourable conformation in order to form a complex with periodate. In agreement, it was found that 1 : 6-anhydro-D-allopyranose,[13] in which the conformation with two axial hydroxyl groups is obligatory, behaved exactly as other complex-forming triols. Consequently, the behaviour of mannose needs further consideration.

β-D-Mannose is the only compound we have examined having a potential *cis-cis*-1 : 2 : 3-triol system in a six-membered ring which does not form a complex with periodate. We believe this to be due to the reluctance of the compound to adopt the necessary conformation. Reeves [9] predicted that both conformations will normally be present in this sugar, but we feel that the method of assessing relative stabilities suggested by Reeves is based on an arbitrary allotment of significance to the various factors. We therefore put forward what we believe to be a more accurate method of assessment.

The Stabilities of the Conformations of Pyranose Rings.—Reeves [14] gave strong evidence for excluding all but the two " chair " conformations of pyranose rings and only these two conformations will be considered in this discussion. It is assumed that the degree of distortion in a molecule is determined by the total amount of overlap of non-bonded atoms, overlap between each pair being calculated separately and added together. In considering each pair of atoms, it is assumed that the other atoms in the molecule are not displaced from their normal positions. This assumption, though necessary for calculations, is not strictly justified since overlap between one pair of atoms will result in the readjustment of the positions of all the atoms in the molecule. The following atomic dimensions have been used: C–C bond, 1·54 Å; C–H bond, 1·07 Å; C–O bond, 1·43 Å; [15] van der Waals radius of carbon, 1·60 Å; [16] hydrogen, 1·20 Å (see below); oxygen, 1·40 Å.[15] It has been assumed that all the carbon and oxygen valency angles are 109° 28′. This is the usual value taken for the carbon valency angle in calculations of this kind, although in propane the angle is 111·5°.[17] Similarly, the oxygen valency angle in dimethyl ether is 111°,[18] but an alteration of approximately 2° in the values taken does not affect the conclusions to be drawn later.

On the above basis, we have calculated values for the overlaps of various pairs of atoms in the pyranose forms of sugars (see Table 2). From these values the difference between the total overlaps for the 1C and C1 conformations of each compound concerned have been calculated. Thus in the case of β-D-glucose, the pertinent interactions in the C1 conformation are between $H_{(O\text{-}1)}$ and $C_{(5)}$, $C_{(1)}$ and $H_{(C\text{-}5)}$, $C_{(6)}$ and $O_{(O\text{-}4)}$, $C_{(6)}$ and $H_{(O\text{-}4)}$, $H_{(O\text{-}5)}$ and $C_{(3)}$, $C_{(5)}$ and $H_{(O\text{-}3)}$, $H_{(O\text{-}4)}$ and $C_{(2)}$, $C_{(4)}$ and $H_{(O\text{-}2)}$, $H_{(O\text{-}3)}$ and $C_{(1)}$, $C_{(3)}$ and $H_{(O\text{-}1)}$, $H_{(O\text{-}1)}$, and $H_{(O\text{-}5)}$. In the 1C conformation, interactions to be considered occur between $O_{(O\text{-}1)}$ and $C_{(5)}$, $C_{(1)}$ and $C_{(6)}$, $C_{(6)}$ and $C_{(3)}$, $C_{(6)}$ and $H_{(O\text{-}4)}$, $C_{(5)}$ and $O_{(O\text{-}3)}$, $O_{(O\text{-}4)}$ and $C_{(2)}$, $C_{(4)}$ and $O_{(O\text{-}2)}$, $O_{(O\text{-}3)}$ and $C_{(1)}$, $C_{(3)}$ and $O_{(O\text{-}1)}$, $O_{(O\text{-}1)}$ and $C_{(6)}$, $C_{(6)}$ and $O_{(O\text{-}3)}$, $O_{(O\text{-}3)}$ and $O_{(O\text{-}1)}$, $O_{(O\text{-}2)}$ and $O_{(O\text{-}4)}$. Interactions between atoms within the rings are omitted since they are the same in both conformations. The differences in total overlap between the 1C and C1 conformations are listed in Table 1

[13] Pratt and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 1906.
[14] Reeves, *ibid.*, 1950, **72**, 1499.
[15] Pauling, " The Nature of the Chemical Bond," Cornell Univ. Press, 1948, p. 164.
[16] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 173.
[17] Pauling and Brockway, *J. Amer. Chem. Soc.*, 1937, **59**, 1223.
[18] Klyne in " Progress in Stereochemistry," Butterworths, London, 1954, p. 364.

TABLE 2. *Overlap of pairs of atoms in the chair conformations of the pyranose ring.*

Substituents (a = axial; e = equatorial) Interactions between		Overlap (Å)	Interactions between ring atom and subst.		Overlap (Å)
H and H			O		
1a	5a	0·19	$C_{(3)}$	1a	0·33
O and O			$C_{(3)}$	3a	0·03
2a	3e	0·04	$C_{(4)}$	2a	0·03
2e	3a	0·04	$C_{(3)}$	1a	0·10
3a	4e	0·04	$C_{(2)}$	4a	0·03
3e	4a	0·04	$C_{(1)}$	3a	0·03
1a	3a	0·19	H		
2a	4a	0·11	$C_{(1)}$	5a	0·28
H and O			$C_{(2)}$	1a	0·06
1a	5a	0·38	$C_{(3)}$	5a	0·06
5a	1a	0·38	C		
C and H			$C_{(1)}$	5a	0·47
5a	1a	0·56	$C_{(3)}$	5a	0·25
5a	3a	0·17			
5a	4a	0·06			
5e	4a	0·07			
5e	4e	0·06			
C and O					
5a	1a	0·83			
5a	3a	0·38			
5a	4e	0·11			
5e	4a	0·11			
5e	4e	0·10			

(column *B*). It must be emphasised that these figures are intended only to be used to arrange the compounds in the correct order of stabilities of the two conformations. For those compounds having a high value for the difference, the C1 conformation is preferred; those in the middle range are expected to change readily from one conformation to the other; a negative value for the difference implies that the 1C conformation is the more stable. Predictions on this basis, in many cases, agree with those of Reeves.[19] The chief exceptions are as follows: We consider β-D-altrose, β-D-mannose, and β-D-talose to be appreciably less stable in the 1C conformation. α-D-Lyxose now appears to favour the C1 conformation. We consider α-D-allose, β-D-ribose, and α-D-xylose to favour the 1C rather than the C1 conformation.

It is seen that the new method satisfactorily predicts that, of those sugars having a potential *cis-cis*-1 : 2 : 3-triol system, mannose is the least likely to take up the conformation necessary for complex formation with periodate. Furthermore, each compound which forms a complex can do so without adopting a highly unfavourable conformation. For instance, although in β-D-talose the C1 conformation is preferred this sugar is able to form complexes in both conformations. α-D-Ribose also can do this but β-D-ribose can form a complex only in the 1C conformation. It is impossible to state whether ribose forms its complex in the slightly less favourable conformation of the β-form, or in the more favourable α-form. These alternatives serve to emphasise the point made earlier that it is not satisfactory to regard crystalline ribose necessarily as β-D-ribopyranose. The α-D-ribopyranose structure could equally explain the properties of the natural sugar.

Further justification for the method of analysis, put forward for comparing stabilities of different chair conformations, is provided by the formation of 1 : 6-anhydrohexopyranoses in acid solution. The formation of these anhydrides necessitates the adoption of the 1C conformation by the β-form of the sugar. In Table 1 (column C) are listed the percentages of anhydride in equilibrium with the hexose sugar in acid solution, and it is seen that there is good inverse correlation between these figures and the differences in overlap between the 1C and the C1 form of the β-hexoses. Thus a small amount of

[19] Reeves, *Adv. Carbohydrate Chem.*, 1951, **6**, 107.

TABLE 3. *Uptake of periodate (mol.).*

No.	Compound	Buffer	Uptake at time (min.) 1	2·5	5	10	15	20	25	30	40	60	120	240
1	β-D-Ribose	A	2·03	2·55	2·88	3·42	3·70	—	3·94	—	4·05	4·06	—	—
2	β-D-Ribose	D	0·33	0·38	—	—	0·56	—	—	1·06	—	—	2·20	3·99
3	β-D-Ribose	E	0·93	—	—	2·29	—	3·06	—	3·60	—	4·19	—	—
4	β-D-Ribose	C	1·28	1·42	1·68	2·12	2·80	—	—	3·53	—	—	4·19	4·20
5	β-D-Ribose	F	1·12	—	—	—	—	1·80	—	—	2·18	2·95	3·74	4·04
6	β-D-Ribose	G	1·09	—	1·12	—	—	1·38	—	—	1·52	—	2·26	4·04
7	β-D-Ribose	B	1·27	1·27	1·31	1·38	—	—	—	—	1·75	—	—	3·39
8	β-D-Lyxose	B	1·35	1·53	—	2·06	—	2·67	—	3·23	—	3·72	4·02	—
9	α-D-Xylose	B	3·20	3·70	—	3·91	—	3·94	—	—	—	3·97	4·00	—
10	β-D-Arabinose	B	3·57	—	3·8	—	—	3·85	—	—	—	3·94	4·10	—
11	α-D-Glucose	B	3·04	3·85	—	4·74	—	4·88	—	—	—	4·94	—	5·07
12	α-D-Galactose	B	3·77	3·86	—	4·11	—	4·35	—	—	—	4·68	4·90	5·07
13	D-Idose	B	5·25	—	—	—	5·30	—	—	—	—	—	—	—
14	β-D-Altrose	B	—	4·91	4·99	—	—	5·15	—	—	—	5·15	—	—
15	β-D-Mannose	B	3·72	4·27	—	4·86	—	5·02	—	—	—	—	5·04	—
16	D-Gulose–calcium chloride	B	—	1·30	—	2·01	—	2·12	—	—	3·20	—	4·95	—
17	β-D-Talose	B	—	1·07	1·15	—	1·46	—	—	—	1·86	—	2·40	—
18	β-D-Allose	B	—	1·39	—	2·03	2·57	—	—	3·36	—	4·48	5·07	—
19	Ribitol	B	—	3·93	3·93	—	3·93	—	—	—	—	—	—	—
20	*cis-cis-trans-cyclo*Hexane-1 : 2 : 3-triol	B	1·92	2·04	2·07	—	—	—	—	2·07	—	—	—	—
21	*cis-cis-cyclo*Hexane-1 : 2 : 3-triol	B	0·97	0·98	—	1·11	1·21	—	—	1·36	—	1·56	—	—
22	*cis-cis-cyclo*Hexane-1 : 2 : 3-triol	J	0·14	0·14	—	0·18	0·23	—	—	—	—	—	—	—
23	*cis-cis-trans-cyclo*Hexane-1 : 2 : 3-triol	J	1·25	1·36	—	1·63	1·87	—	—	—	—	—	—	—
24	*trans-cyclo*Hexane-1 : 3 : 5-triol	B	0	—	—	0	—	—	—	—	0	—	—	—
25	CH_2Ph β-D-ribopyranoside	B	—	1·03	1·05	1·02	1·00	—	—	1·03	—	—	—	1·09
26	Me β-D-ribopyranoside	B	0·92	0·90	0·89	0·89	—	—	0·94	—	—	—	1·01	1·44
27	Me α-D-lyxopyranoside	B	0·17	—	0·99	—	1·45	—	—	1·86	—	1·99	2·07	2·07
28	Me β-D-xylopyranoside	B	0·04	0·10	—	0·18	0·37	—	—	0·69	—	1·00	—	2·01
29	Me α-D-glucopyranoside	B	0·07	0·17	—	0·28	—	—	—	1·04	—	—	1·80	2·09
30	CH_2Ph β-D-glucopyranoside	B	0·12	0·12	0·10	0·16	0·30	—	—	—	—	—	1·43	2·01
31	Lævoglucosan	B	0·09	0·09	—	0·13	0·23	—	—	—	—	0·55	1·07	1·58
32	1 : 6-Anhydro-D-allopyranose	B	1·25	1·29	—	1·52	—	—	1·79	1·87	2·02	—	—	—
33	*trans-cyclo*Pentane-1 : 2-diol	B *	0·65	0·79	0·90	—	—	0·98	—	—	—	—	—	1·00
34	*cis-cyclo*Pentane-1 : 2-diol	B *	0·96	0·96	0·97	—	0·97	—	—	—	—	—	—	0·99
35	*trans-cyclo*Hexane-1 : 2-diol	B *	0·54	0·75	0·90	0·98	1·02	—	—	—	—	1·02	—	—
36	*cis-cyclo*Hexane-1 : 2-diol	B *	1·00	—	—	1·05	—	—	—	—	—	1·10	—	—
37	5-*O*-Triphenylmethyl-D-ribose	H	2·98	—	3·05	—	3·10	—	—	3·16	—	3·16	—	—
38	5-*O*-Methyl-D-ribose	B	—	2·95	—	2·95	—	—	—	—	—	2·95	—	—
39	CH_2Ph β-D-ribofuranoside	B *	1·03	—	—	1·01	—	1·01	—	—	—	1·06	—	—

All measurements of periodate were done by the arsenite method, except as indicated in D.

A, Unbuffered. B, 0·03M-Phosphate buffer, pH 7. C, 0·02M-Phthalate buffer, pH 6·2. D, 0·03M-Phosphate buffer, pH 7; periodate determined by thiosulphate method. E, 0·02M-Acetate buffer, pH 5·9. F, Phosphate buffer, pH 6·6. G, Phosphate buffer, pH 8·0. H, As in B, but in presence of 50% ethanol. J, As in B, but after standing with sodium tellurate.

* In these experiments, no reappearance of the colour of iodine was observed.

anhydride is found when adoption of the 1C conformation would involve a high total overlap (glucose,[20] galactose,[21] mannose,[22] talose,[23] and allose [13]). On the other hand, the anhydride is readily formed in the cases of gulose,[24] altrose,[20] and idose,[20] in which the relative stability of the 1C conformation is higher. According to Reeves's method of prediction, mannose and talose would be expected to yield more anhydride relative to allose and gulose than is found experimentally.

It has been suggested [25] that 0·6 Å should be taken as an interference value for hydrogen instead of the van der Waals radius of 1·2 Å. If this figure is used, all overlaps involving hydrogen atoms in pyranose rings are eliminated. However, it may be shown that on this basis the order of the sugars given in Table 1 is little affected. The only differences arise with the β-pentopyranoses which appear a little higher in the middle range of the list. None of the conclusions reached is affected.

We consider that the agreement between prediction and experiment justifies our method as a semiquantitative approach to the comparison of different conformations in the series of pyranose sugars. It also adds weight to our claim that the behaviour of ribose and related polyols towards periodate is due to the formation of a complex involving three-point attachment of the ion.

Experimental

Periodate Oxidations.—To a weighed quantity of the material under test (~5 mg.) was added a 0·05N-solution of sodium metaperiodate in water or the appropriate buffer (10 c.c.). All the materials used dissolved immediately and aliquot parts (1 c.c., measured in an " Agla " burette) were added, at intervals, to 0·05N-sodium arsenite containing potassium iodide (2% w/v) and sodium hydrogen carbonate (5% w/v) (1 c.c. measured in an " Agla " burette). The solutions were kept for 15 min., then titrated with 0·1N-iodine (" Agla " burette). Some experiments were also done on ten times this scale with conventional burettes. In both cases, titrations were reproducible within 1%. Owing to the time taken to manipulate burettes, the times of reaction are given to the nearest minute. The results are in Table 3. Results obtained over a protracted experiment with D-ribose are given in Table 4.

Table 4. *Rate of consumption of periodate by* D-*ribose in second phase of the reaction.*

Time (min.)	Periodate consumed (mol.) (*a*)	log (4·13 − *a*)	Time (min.)	Periodate consumed (mol.) (*a*)	log (4·13 − *a*)	Time (min.)	Periodate consumed (mol.) (*a*)	log (4·13 − *a*)
1	1·16	0·47	132	2·81	0·12	300	3·75	−0·42
16	1·45	0·43	170	3·09	0·02	522	4·03	−1·00
36	1·76	0·37	230	3·41	−0·14	630	4·05	−1·09
78	2·29	0·26	275	3·63	−0·30	2050	4·13	—
104	2·57	0·19						

Table 5.

Time of muta-rotation (min.)	Initial uptake of periodate (mol.) D-Ribose	D-Lyxose	Time of muta-rotation (min.)	Initial uptake of periodate (mol.) D-Ribose	Time of muta-rotation (min.)	Initial uptake of periodate (mol.) D-Ribose	D-Lyxose
0·1	1·04	1·00	2·5	1·48	15	1·59	2·9
0·25	1·15	—	5	1·48	25	1·59	2·9
0·5	1·18	2·2	10	1·63	780	1·58	3·2
1·0	1·30	—					

Mutarotation of Ribose in Phosphate Buffer.—D-Ribose (0·0980 g.) was dissolved in phosphate buffer (pH 7·0) (20 c.c.). $[\alpha]_D^{20}$ was −14·5° (1·5 min.), −15·5° (2 min.), −17·5° (3 min.), −18·5° (5 min.), −18·5° (7 min.), −19·5° (10 min.), −20·0° (100 min.).

[20] Stewart and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 424.
[21] Turton, Bebbington, Dixon, and Pacsu, *ibid.*, 1955, **77**, 2565.
[22] Pacsu and Mora, *ibid.*, 1950, **72**, 1045.
[23] See p. .
[24] Stewart and Richtmyer, *J. Amer. Chem. Soc.*, 1955, **77**, 1021.
[25] Braude and Waight in " Progress in Stereochemistry," Vol. I, Butterworths Scientific Publications, London, 1954, p. 146.

ethanol. J. As in B, but after standing with sodium tellurate.
• In these experiments, no reappearance of the colour of iodine was observed.

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Periodate Oxidation after Mutarotation in Water.—The sugar (0·05 g.) was dissolved in water (10 c.c.) at 20° and, after a given time, the solution was added to a solution of sodium metaperiodate (as above) and aliquot parts (10 c.c.) were titrated with sodium arsenite and iodine as described above. This was repeated for various times of mutarotation. The uptake of periodate in each case was plotted against time and the initial rapid uptake was determined by extrapolation to zero time. The results are given in Table 5.

Recovery of Ribose after Treatment with Sodium Metaperiodate.—D-Ribose (0·0402 g.) was added with shaking to a mixture of 0·268M-sodium metaperiodate (1 c.c.), phosphate buffer (pH 7·0) (5 c.c.), and water (4 c.c.) (solution A). After 1 min. an aliquot part of solution A was heated with a solution containing potassium iodide and sodium hydrogen carbonate. No iodine was liberated, indicating the absence of free periodate. Solution A was kept at room temperature for 24 hr. and then chromatographed on paper with butan-1-ol–pyridine–water (10 : 3 : 3) as solvent. The aniline phthalate spray disclosed a dark spot having the same R_F value as ribose run on the same paper and two faint streaks with high R_F values. Aliquot parts of solution A (0·015, 0·020, 0·025 c.c.) were applied to Whatman No. 1 paper and were chromatographed on the same paper as spots containing 25, 50, 75, and 100 μg. of D-ribose. The air-dried paper was dipped in Baar's reagent,[7] excess of the reagent was removed with a rubber roller, and appropriate areas were cut from the paper and the colours determined as described by Baar.[7] A calibration curve was constructed by using the spots containing known amounts of ribose and it was calculated from the results for the three "unknown" spots that the recovery of ribose from the original solution A (10 c.c.) was 27, 24, and 22 mg. respectively.

Change of pH *of Solutions of Sodium Metaperiodate in Presence of Polyols.*—The pH of 0·0048M-sodium metaperiodate (60 c.c.) at 25° was adjusted to the desired value with 0·01N-sodium hydroxide, the polyol (0·387 g.) was added, and the pH was measured at intervals. The results are shown in Table 6.

TABLE 6. *Changes of* pH *during periodate oxidation of* cis-trans- *and* cis-cis-cyclo*hexane*-1 : 2 : 3-*triol at various initial* pH.

Compound	pH at time (min.) 0	1	2	5	10	20	40	60
cis-trans-	7·99	8·03	8·24	8·44	8·67	8·94	9·03	9·06
cis-trans-	9·69	9·70	9·84	10·14	10·24	—	10·69	—
cis-cis-	7·26	5·86	5·85	5·90	6·25	6·51	—	—
cis-cis-	8·66	7·80	7·29	7·02	7·22	7·56	8·00	—
cis-cis-	9·09	8·78	8·62	8·41	8·35	8·44	8·58	8·63

Change of pH *of Sodium Tellurate Solutions in Presence of Polyols.*—0·0032M-Telluric acid (25 c.c.) at 25° was adjusted to pH 8·0 with 0·01N-sodium hydroxide. The polyol was added and the pH was measured at intervals. The results are shown in Table 7.

TABLE 7. *Changes of* pH *of solutions of sodium tellurate in presence of various polyols.*

Compound added	pH at time (min.) 0	5	20	30	60	120
D-Ribose	8·00	7·75	—	7·28	—	6·46
D-Glucose	7·99	7·86	—	7·80	7·80	7·78
D-Lyxose	7·99	—	7·57	6·88	—	6·41
D-Xylose	8·02	7·82	7·71	7·67	7·65	—
D-Arabinose	7·97	7·80	—	7·58	—	7·35
Me β-D-ribopyranoside	7·98	—	7·41	7·11	—	6·54
Me α-D-glucopyranoside	7·98	7·85	—	7·81	7·81	7·77

Action of Dilute Acid on D-*Talose.*—D-Talose (0·025 g.) was heated at 100° for 5 hr. with N-hydrochloric acid (5 c.c.). Chloride ions were removed with silver carbonate and the solution was concentrated and chromatographed on paper with butan-1-ol–water. The paper was sprayed with ammoniacal silver nitrate and a spot (R_F 0·1) corresponding to talose was observed together with some slow-moving material which probably contained polysaccharide. No

material moving faster than talose, as would be expected if an anhydride were formed, was detected.

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120. *Ketose–Polyol Interconversions by a Ropy-cider Organism.*

By S. A. BARKER, E. J. BOURNE, E. SALT, and M. STACEY.

The specificity of the ropy-cider organism in the ketose ⇌ polyol reaction is described. It is suggested that the required conformation of the ketose is the 1C chair form of the pyranose ring with the 3-hydrogen atom and the 5-hydroxyl group axial. Polyols with the carbon skeleton written in the zig-zag form require the 2- and the 5-hydroxyl groups and the 3-hydrogen atom to be directed below the plane of the paper. The examination of a cell-free extract of the enzyme responsible is described.

PREVIOUS work [1] has shown that the major carbohydrate change effected by a *Lactobacillus* causing ropiness in cider is the conversion of the fructose present into mannitol. The specificity of resting cells of the *Lactobacillus* with respect to both the ketose and the polyol, together with an examination of the enzyme responsible, are the subjects of the present communication.

To determine the optimum pH of the reaction, equal amounts of the resting cells were incubated with 3% of fructose in phosphate and tri(hydroxymethylamino)methane buffers at pH's between 4 and 8. The optimum conversion of fructose into mannitol occurred in phosphate buffer of pH 8. Further comparisons showed that the fructose → mannitol conversion was effected equally well at 30° under aerobic and anaerobic conditions, but faster at 30° than at 25°.

In these optimum conditions (pH 8 and 30°) other ketoses were tested as possible substrates for resting cells of the ropy-cider organism (Table 1). Of those which were converted into their corresponding polyols, D-fructose, perseulose (L-*gala*heptulose), dihydroxyacetone written as the dimer,[2] and 2-keto-D-gluconic acid all have the 3-hydrogen atom and the 5-hydroxyl group axial in the 1C conformation (I), which should be the preferred conformation in each case. D-*manno*Heptulose and D- and L-*gluco*heptulose which do not show these features were unsuitable substrates. The position of L-sorbose is in doubt: in two early incubations sorbose did not act as a substrate for resting cells although this batch of cells effected the fructose → mannitol conversion; in two later tests the formation of a component with the same R_F value and staining properties as sorbitol was observed; in a larger-scale incubation, however, there was no trace of this product. The conversion of 2-keto-L-gulonic into L-gulonic acid also appeared anomalous and in this connexion it is interesting that L-sorbose and 2-keto-L-gulonic acid have closely related structures, which differ from that shown in (I).

Anaerobic incubation of mannitol and resting cells alone in various buffers (pH 6—9) or incubation under aerobic conditions at both 25° and 30° did not produce fructose. Some success was obtained on addition of diphosphopyridine nucleotide (DPN) but the equilibrium appeared to lie heavily on the mannitol side. As an alternative, mannitol and resting cells were incubated with dihydroxyacetone; it was hoped that DPN formed *in situ* by reduction of the dihydroxyacetone would act as coenzyme in the oxidation of the mannitol. Such a system was found to produce fructose and glycerol. Other polyols were tested under similar conditions with DPN, with DPN + Methylene Blue,

[1] Barker, Bourne, Salt, and Stacey, *J.*, 1958, 2736.
[2] Whitmore, "Organic Chemistry," 2nd Edn. D. van Nostrand, Co. Inc., 1951, p. 462.

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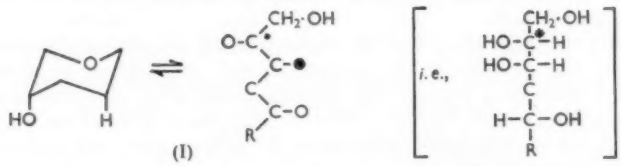
with dihydroxyacetone, or with fructose. The results (Table 2) showed that the enzyme required the polyol substrate to have the structure which is illustrated in (I) in two ways: first, in the usual Fischer convention and, secondly, in the planar zig-zag form described by Barker, Bourne, and Whiffen.[3] It will be seen that, in the zig-zag form, the 2- and the 5-hydroxyl group and the 3-hydrogen atom are directed below the plane of the paper (I). There were no exceptions to this conclusion. Volemitol, having the proposed configuration at both ends of the molecule, would be expected to give two heptuloses, D-*manno*heptulose and sedoheptulose. In two cases a component with the same R_F value as D-*manno*heptulose was formed and a trace of a second component with a slightly higher R_F was noted. No sedoheptulose was available as a reference. The position of L-fucitol is doubtful but in two cases an unidentified component with R_G *ca.* 2·2 was produced. Here the polyol has the required structure if the methyl group can be regarded in the same way as H, as is the case with the enzyme from *A. suboxydans*.

Thus independent studies of the specificity requirements in ketose and polyol substrates have both led to the conclusion that the important positions are 3 and 5, in addition of course to position 2 which is the site of the oxidation–reduction process. Presumably the hydrogen or hydroxyl groups at these positions serve as points of attachment for the enzyme. This attachment could involve $(OH)^3$–$(OH)^5$, $(OH)^3$–H^5, H^3–H^5, or H^3–$(OH)^5$. In the first three cases, however, the distances separating these groups are markedly different in the ketose from those in the zig-zag form of the polyol. In the last case they

Required conformations for ketose–polyol interconversion.



* Site of oxidation. O = Oxygen down. ● = Oxygen up.

are identical at 2·54 Å, which is slightly greater than the distance separating two axial oxygen atoms [4] in a pyranose ring or two βC oxygen atoms in a polyol.[3] Moreover, models showed that it is possible to interconvert the chair and the zig-zag structure shown in (I) without significantly altering the H^3–O^5 distance at any stage; this change is in fact equivalent to the interconversion of chair and boat forms. We conclude that the oxidation–reduction process proceeds by a route which is basically in agreement with that proposed by Edson [5] for the oxidation of sorbitol by rat-liver polyol dehydrogenase. The requisite structures of the ketose and polyol substrates shown in (I) were determined independently, but they show close agreement. In the present case, it is suggested that each polyol forms a complex with the enzyme through H^3 and O^5 of its zig-zag form, which during the oxidation closes to give the pyranose-ring form of the ketose. This proposed mechanism explains the fact that reduction of dihydroxyacetone to glycerol is not reversible, if it is assumed that the dimer of dihydroxyacetone, in the chair form, acts as substrate. It explains also why D-*manno*heptulose, produced in the oxidation of volemitol, is not itself a substrate, because in this case the C1 conformation would be strongly favoured over the 1C conformation demanded by the enzyme.

Since experiments with resting cells suggested that the interconversion of fructose and mannitol proceeds by the reaction:

$$\text{Fructose} + \text{DPNH} + \text{H}^+ \rightleftharpoons \text{Mannitol} + \text{DPN}^+$$

[3] Barker, Bourne, and Whiffen, *J.*, 1952, 3865.
[4] Klyne, "Progress in Stereochemistry," Butterworth Scientific Publications, 1954, Vol. I, p. 36.
[5] Edson, Australian and New Zealand Association for the Advancement of Science, 1953, Vol. 29, p. 281.

a spectrophotometric method [6] of testing activity in various enzyme fractions was adopted. Incubation of a cell-free extract of the ropy-cider organism with DPNH alone was accompanied by a rapid fall in absorption at 340 mμ. Such activity might have been due to a DPNH oxidase. The use of a known [7] DPNH oxidase inhibitor (2-heptyl-4-hydroxyquinoline *N*-oxide), dialysis, precipitation with acetone, or fractionation with ammonium sulphate did not prevent the fall in absorption.

Two methods were successful in eliminating this spurious activity. The supernatant solution from a cysteine precipitation of a cell-free extract was found to cause little decrease (0·02 in 20 min.) in optical density (340 mμ) when incubated with DPNH alone. The addition of fructose, however, produced a large decrease (0·151 in 20 min.). Since examination of the ultraviolet spectrum of the material precipitated by cysteine suggested that it contained nucleic acid, it was decided to test protamine sulphate in the purification, since this is known [8] to precipitate nucleic acid. Before the addition of protamine sulphate, the cell-free extract was precipitated with ammonium sulphate at 30% and 65% saturation and each fraction dialysed against a glycine buffer of pH 5·9. The fraction obtained at 65% saturation, when treated with protamine sulphate, gave a supernatant solution which showed virtually no endogenous oxidation even after addition of cysteine. Addition of fructose, however, caused a large drop (0·579 in 110 min.) in optical density at 340 mμ and the solution was found to contain mannitol and glycerol. The latter probably resulted from the presence of a small aldolase impurity which, acting on the fructose, gave dihydroxyacetone which was later reduced to glycerol.

Another enzyme fraction obtained by protamine sulphate precipitation without prior ammonium sulphate fractionation was inactive in the absence of cysteine, showed appreciable endogenous oxidation, and appeared to contain large amounts of aldolase since the sole polyol detected on incubation with fructose was glycerol. Addition of *p*-chloromercuribenzoate to an equilibrium mixture of this enzyme fraction and DPNH caused an increase in absorption at 340 mμ. This suggests that some of the added DPNH is bound by the enzyme, giving a complex that does not absorb markedly in the 300—380 mμ region, and that bound DPNH is liberated on addition of *p*-chloromercuribenzoate. Such enzyme–coenzyme complexes have been discussed in detail by Velick.[9] The enzyme fraction was also inactivated by *p*-chloromercuribenzoate, and reactivated on addition of cysteine, suggesting that thiol groups may be essential for its activity.

Experimental

Preparation of Resting Cells.—A sterile medium containing magnesium sulphate (0·2%), sodium nitrate (0·2%), ammonium sulphate (0·2%), ascorbic acid (0·3%), dialysed yeast extract (1·0%), and fructose (9·06%) was inoculated with the ropy-cider organism and incubated for 11—14 days at 30° in a vacuum-desiccator (4 cm. Hg) with a vessel containing 25% sodium hydroxide solution and pyrogallol. The cells were collected, washed with water, dialysed overnight, and freeze-dried.

Conditions for the Fructose → Mannitol Conversion.—Equal amounts of resting cells were separately incubated in sterile tubes with 3% solutions of fructose in various buffers at 30° under anaerobic conditions. At intervals, aliquot parts from each were analysed and estimated visually on paper chromatograms irrigated with the upper layer of a butan-1-ol–ethanol–water–ammonia mixture (40 : 10 : 49 : 1). The results after 11 days were:

0·083M-Tri(hydroxymethylamino)methane "Tris"	pH 4·7	6·4	7·1	8·0
Amount of mannitol formed	None	Trace	Trace	*ca.* 25%
0·02M-Phosphate	pH 4·8	6·4	7·1	8·0
Amount of mannitol formed	*ca.* 25%	*ca.* 25%	*ca.* 50%	*ca.* 50%

Equal amounts of resting cells were separately incubated aerobically with 3% fructose solutions in 0·02M-phosphate buffer (pH 8) at 25° and 30°. Paper chromatography showed

[6] Racker, *J. Biol. Chem.*, 1949, **177**, 883.
[7] Lightbown and Jackson, *Biochem. J.*, 1956, **63**, 130; **62**, 16.
[8] Alexander, *Biochim. Biophys. Acta*, 1953, **10**, 595.
[9] Velick, "Mechanism of Enzyme Action," Johns Hopkins Press, Baltimore, 1954, p. 491.

that complete conversion of fructose into mannitol was effected in 5 days at 30° and in 6 days at 25°. An identical digest incubated anaerobically at 30° gave the same result.

Substrate Specificity in the Ketose ⟶ Polyol Conversion.—Freeze-dried cells (*ca.* 20 mg.) were incubated with solutions of various ketoses (1—2%) in 0·03M-phosphate buffer (pH 8·0; 1 c.c.) under anaerobic conditions at 30°, and analysed as above. The results are given in Table 1.

Conditions for the Mannitol ⟶ Fructose Conversion.—Equal quantities of resting cells were incubated anaerobically at 30° with 3% of mannitol in 0·02M-phosphate buffer at pH 6·4, 7·2, 8·0, and 9·0 and in 0·08M-" Tris " buffer at pH 7·2, 8·0, and 9·0. Chromatography of samples, taken at intervals over a period of 14 days, showed no production of fructose. Similar experiments under aerobic conditions and at both 25° and 30°, using 0·02M-phosphate buffer (pH 8·0), gave no fructose. Of five experiments in which resting cells (19—35 mg.) were incubated aerobically with mannitol (11—12 mg.) in phosphate buffer (pH 8—10; 1 c.c.) at 30°, in the presence of added diphosphopyridine nucleotide (30 mg.; 34% of DPN), three digests showed partial conversion into fructose within 7—8 days, while the other two contained only

TABLE 1. *Ketose ⟶ polyol conversions.*

Substrate	Substrate (mg.)	Resting cells (mg.)	Incubation time (days) *	Reduction product formed
L-*gala*Heptulose	10	38	5P, 9	Perseitol
,, ...	12	30	5P, 7	Perseitol
D-*manno*Heptulose.....	8	21	7	None
,, ...	10	17	9	None
D-*gluco*Heptulose	10	25	7	None
,, ...	7	21	7	None
L-*gluco*Heptulose	10	23	7	None
,, ...	8	24	7	None
D-Fructose	30	1	3C, 6	Mannitol
,, ...	20	9·3	2C, 9	Mannitol
,, ...	20	22	3C, 7	Mannitol
L-Sorbose	30	8	6	None
,, ...	20	17	9	None
,, ...	21	24	7C	Sorbitol
,, ...	20	21	7C	Sorbitol
,, ...	200	100	7	None
2-Keto-D-gluconic acid ...	17	19	5P, 7	Hexonic acid
2-Keto-L-gulonic acid ...	13	18	5P, 7	Gulonic acid
Dihydroxyacetone	20	21	2P, 9	Glycerol

* P = Partial conversion. C = Complete conversion.

traces of fructose after the same time. No fructose was detected in controls in which either the mannitol or the resting cells were omitted from the system. Incubation of mannitol (11 mg.) and dihydroxyacetone (11 mg.) in 0·03M-phosphate buffer (1·0 c.c.) with resting cells (19 mg.) aerobically at 30° gave fructose and glycerol.

Substrate Specificity in the Polyol ⟶ Ketose Conversion.—Resting cells (*ca.* 20 mg.) were incubated for 7—8 days aerobically at 30° with 1—2% solutions of various polyols (1 c.c.) in 0·03M-phosphate buffer (pH 8; 1 c.c.) with added diphosphopyridine nucleotide (*ca.* 30 mg.; 34% of DPN). In some cases 1% of Methylene Blue (0·2 c.c.) was also added. The same polyols were also incubated for 7 days aerobically at 30° with resting cells (20—30 mg.) in the presence of dihydroxyacetone or fructose. The positive results are given in Table 2. With other polyols tested (sorbitol, L-glucitol, dulcitol, D-arabitol, ribitol, xylitol, *meso*-erythritol, glycerol), only the reduction products (mannitol or glycerol) of the added fructose or dihydroxyacetone were detected.

Preparation of a Cell-free Extract.—Freeze-dried cells, together with an equal volume of glass beads, were suspended in 0·03M-phosphate buffer (pH 8·0) and smashed in a Mickle disintegrator, working at maximum efficiency, for 1 hr. at 0°. The glass beads and most of the cell debris were removed by centrifugation at 0°. The cell-free extract so obtained was used immediately or freeze-dried.

Assay of Activity.—Diphosphopyridine nucleotide (DPN) (2·172 g.) was isolated from

baker's yeast (12 lb.) by the method of Nielands and Åkeson.[10] The amount of DPN in this product, determined [11] spectrophotometrically by the cyanide method, was 33·8%. A portion (0·257 g.) of the crude DPN was converted [12] into DPNH by treatment with sodium dithionite. The product (0·115 g.) was found by spectrophotometric measurement [13] to contain 59% of DPNH. Other samples of DPN and DPNH were purchased from Sigma Ltd.

TABLE 2. *Polyol → ketose conversions.*

Substrate and wt. (mg.)	Hydrogen acceptor added: DPN (mg.)	Others (mg.) †	Products detected
Perseitol, 9	23 *	—	Perseulose, 3rd day, P
Perseitol, 10	30	M.B., 2	Perseulose, 3rd day, P
Perseitol, 9	—	D.H.A., 10	Perseulose + glycerol
Volemitol, 11	33	M.B., 2	*manno*Heptulose, 2nd day, P
Volemitol, 5	30	—	*manno*Heptulose, 3rd day, P; 2nd component, 7th day
Volemitol, 11	—	D.H.A., 10	*manno*Heptulose + 2nd component + glycerol
β-Sedoheptitol, 15	30	—	Heptulose, 5th day
β-Sedoheptitol, 5	42	—	Heptulose, 4th day
β-Sedoheptitol, 11	—	D.H.A., 10	Heptulose + glycerol
D-Talitol, 10	30	—	Hexulose, 3rd day
D-Talitol, 6	30	M.B., 2	Hexulose, 3rd day
D-Talitol, 10	—	D.H.A., 10	Hexulose (trace) + glycerol
L-Fucitol, 11	30	—	Component of R_G *ca.* 2·2
L-Fucitol, 11	—	D.H.A., 10	Glycerol only
L-Fucitol, 14	—	Fructose, 10	Component of R_G *ca.* 2·2 + mannitol

* Pure DPN added. † M.B. = Methylene Blue; D.H.A. = dihydroxyacetone; P = partial conversion.

The enzyme fraction (equivalent to 1 c.c. of cell-free extract) in 0·03M-phosphate buffer (pH 8; 1·5 c.c.) and DPNH solution (200 μg. in 0·5 c.c. of buffer) were pipetted into a silica cell (1 cm.). The control cell was filled with phosphate buffer and the ultraviolet spectra were measured between 240 and 390 mμ. Fructose solution (3·6 mg. in 0·5 c.c. of buffer) was added, and the decrease in absorption at 340 mμ used as a measure of enzyme activity.

When assayed by this method the cell-free extract exhibited apparent activity when incubated with DPNH alone.

Similar results were obtained when either dialysed cell-free extract or the precipitate obtained on addition of acetone (3 vol.) at 0° to cell-free extract was used. This activity was still exhibited by enzyme fractions precipitated at 0° with ammonium sulphate at 36·4% saturation and at 67·7% saturation, as well as by that remaining in the supernatant liquid. Such activity in the cell-free extract was not inhibited by 2-heptyl-4-hydroxyquinoline *N*-oxide (7 μg.), a known DPNH oxidase inhibitor.[7] Incubation of the cell-free extract with DPNH in an atmosphere of nitrogen caused no improvement.

Elimination of Spurious Activity from the Cell-free Extracts.—(1) *By cysteine.* Freeze-dried extract (47·5 mg.) was redissolved in water (5 c.c.), and cysteine hydrochloride (48·6 mg.) added. After 2 hr. at 0°, the flocculent precipitate was centrifuged off and the supernatant solution tested for activity.

With DPNH alone the decrease in absorption at 340 mμ was slight (0·02 in 20 min.) but in the presence of fructose there was a decrease of 0·151 in 20 min.

The precipitate formed on the addition of cysteine was dissolved in dilute sodium hydroxide, and the solution dialysed overnight against running tap-water. The solution then showed a broad peak at 260 mμ, the ratio of the optical density 280 : 260 mμ being 0·56.

(ii) *By protamine sulphate.* To a cell-free extract (20 c.c.), solid ammonium sulphate was added to give 30% saturation. The suspension was adjusted to pH 8 with ammonia and left at 0° for 5 hr. The precipitate was recovered by centrifugation, dissolved in phosphate buffer

[10] Nielands and Akeson, *J. Biol. Chem.*, 1951, **188**, 307.
[11] Colowick, Kaplan, and Ciotti, *J. Biol. Chem.*, 1951, **191**, 447.
[12] "Biochemical Preparations," Chapman and Hall Ltd., 1952, Vol. II, p. 92.
[13] Horecker and Kornberg, *J. Biol. Chem.*, 1948, **175**, 385.

XUM

(5 c.c.), and dialysed against the same buffer (250 c.c.) and then water (2 × 250 c.c.). To the supernatant solution (23 c.c.) more ammonium sulphate was added to give 65% saturation. After being left overnight at 0° the precipitate obtained was treated as before. The supernatant solution was dialysed at 0° against phosphate buffer (600 c.c.) and water (2 × 600 c.c.). To all these fractions, 1·8% protamine sulphate solution was added until no further precipitate was formed. After centrifugation, each supernatant solution was dialysed against three changes of 0·1M-glycine–hydrochloric acid buffer (pH 5·9) for 48 hr. at 0°. Each solution was freeze-dried. The fraction (A) (0·166 g.) precipitated at 65% saturation and that (B) (0·182 g.) obtained from the supernatant liquid were tested for enzyme activity.

Each fraction (A, 22 mg.; B, 25 mg.) in 0·1M-glycine–hydrochloric acid buffer (pH 5·9; 2·6 c.c.) was mixed with DPNH (800 μg.) in glycine buffer (0·2 c.c.) and transferred to a silica cell (1 cm.), glycine buffer being used in the control cell. No decrease in the absorption at 340 mμ was observed; cysteine hydrochloride (400 μg.) in glycine buffer (0·2 c.c.) was added and the decrease in absorbance was noted. When equilibrium was reached, fructose (170 μg.) in glycine buffer (0·1 c.c.) was added and the decrease in absorption (optical density) was again noted.

	A	B
Endogenous oxidation, decrease in absorption at 340 mμ	Negligible	0·848 in 77 min.
Fructose added, decrease in absorption at 340 mμ after 2 min.....	0·213	0·005
Fructose added, total decrease in absorption at 340 mμ	0·579 in 110 min.	0·321 in 4 hr.

To the test solutions, two volumes of acetone were added to remove protein. After removal of acetone, the aqueous solutions were passed down Amberlite IRA-400 columns to remove fructose.[1] The effluents were concentrated, freeze-dried, and examined by paper chromatography. Both mannitol and glycerol were detected.

Inhibition of Enzyme Activity by p-*Chloromercuribenzoate.*—An enzyme fraction obtained from the cell-free extract by removal of spurious activity with protamine sulphate without prior ammonium sulphate precipitation was dialysed against 0·03M-phosphate buffer (pH 8) and freeze-dried. The enzyme fraction (31 mg.) in water (1 c.c.) and DPNH solution [240 μg. in 0·03M-phosphate buffer of pH 8 (1·4 c.c.)] were transferred to a silica cell (1 cm.). The mixture showed no decrease in optical density at 340 mμ. On the addition of cysteine hydrochloride (410 μg. in 0·07 c.c. of buffer) a decrease of 0·28 in absorption at 340 mμ in 35 min. was observed. After equilibrium was reached, the addition of *p*-chloromercuribenzoate (620 μg. in 0·2 c.c.) resulted in a gradual increase (0·10 in 70 min.) in the optical density at 340 mμ. When the optical density reached a steady maximum, fructose (3·5 mg. in 0·5 c.c. of buffer) was added. There was a decrease in absorption due to dilution but no further decrease was observed until cysteine hydrochloride (1·17 mg. in 0·5 c.c. buffer) was added. Then absorption at 340 mμ fell by 0·12 in 30 min. Analysis of the reaction solution, after removal of as much protein, phosphate, and fructose as possible, revealed the presence of glycerol.

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121. *Cyclic Keto-amines. Part IV.*[1] *The Synthesis and Reactions of* 1 : 2 : 3 : 4-*Tetrahydro-2-methyl-4-oxo*isoquinoline.

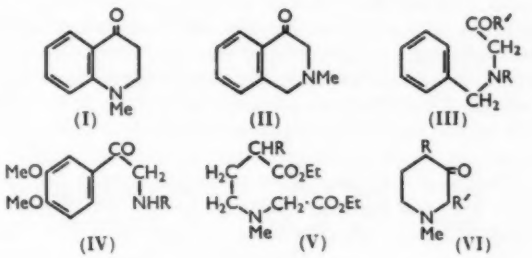
By I. G. Hinton and Frederick G. Mann.

The above *iso*quinoline has been synthesised in order to investigate the chemistry of this novel type of *iso*quinoline derivative, and to compare it with that of the isomeric tetrahydro-1-methyl-4-oxoquinoline. The condensation product of ethyl *o*-chloromethylbenzoate and the ethyl ester of sarcosine has been subjected to a Dieckmann cyclisation, giving 3-ethoxycarbonyltetrahydro-2-methyl-4-oxo*iso*quinoline, which with hot acid underwent hydrolysis and decarboxylation to give the required oxo*iso*quinoline.

Salts of the oxo*iso*quinoline are stable, but the liquid base is readily oxidised by the air, ultimately to *N*-methylphthalimide. The base and its salts in solution undergo dehydrogenation even at room temperature, to give the 4-hydroxy-2-methyl*iso*quinolinium cation. This strong tendency to aromatise the heterocyclic ring is also shown by salts of the phenylhydrazone of the oxo*iso*quinoline, which readily undergo dismutation in acid solution to the corresponding salts of the 4-amino-2-methyl*iso*quinolinium cation and aniline. The semicarbazone similarly gives the same cation.

Other reactions of the oxo*iso*quinoline and of its 3-ethoxycarbonyl derivative are discussed.

The synthesis and reactions of 1 : 2 : 3 : 4-tetrahydro-1-methyl-4-oxoquinoline (I) and its 1-phenyl analogue have been extensively investigated,[2] and we have extended these studies to the reactions of 1 : 2 : 3 : 4-tetrahydro-2-methyl-4-oxo*iso*quinoline (II). Previous attempts to synthesise compounds of type (II) have failed: for example, the cyclisation of the hydrochloride of *N*-benzyl-*N*-methylglycyl chloride[3] (III; R = Me,



R′ = Cl) with aluminium chloride, or of *N*-benzyl-*N*-toluene-*p*-sulphonylglycine[4] (III; R = SO_2·C_6H_4Me, R′ = OH) with phosphoric anhydride, failed. Attempted Bischler–Napieralski cyclisation of compounds such as *N*-(phenylacetyl)phenacylamine,[5] Ph·CO·CH_2·NH·CO·CH_2Ph, with phosphorus oxychloride gave oxazoles; and cyclisation of 3 : 4-dimethoxyphenacylamine (IV; R = H) with formaldehyde or of the *N*-formyl derivative (IV; R = ·CHO) with phosphorus oxychloride also failed.[6] The action of primary amines on *o*-chloromethylphenacyl chloride, Cl·CH_2·C_6H_4·CO·CH_2Cl, gave *iso*indolines (see following paper).

[1] Part III, Ittyerah and Mann, *J.*, 1958, 467.
[2] R. C. Cookson and Mann, *J.*, 1949, 67; Mann, *J.*, 1949, 2816; Allison, Braunholtz, and Mann, *J.*, 1954, 403; Braunholtz and Mann, *J.*, 1955, 381; 1957, 4166; 1958, 3368; cf. also ref. 1.
[3] Mannich and Kuphal, *Ber.*, 1912, **45**, 314.
[4] Clemo and Perkin, *J.*, 1925, **127**, 2297.
[5] Robinson, *J.*, 1909, **95**, 2167; Young and Robinson, *J.*, 1933, 275.
[6] Campbell, Haworth, and Perkin, *J.*, 1926, 32.

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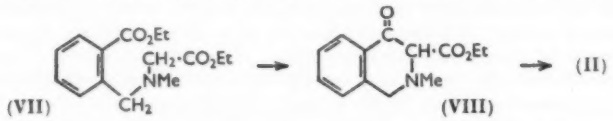
McElvain *et al.*[7] have shown, however, that the ethyl ester of *N*-(3-ethoxycarbonylpropyl)sarcosine (V; R = H) is cyclised by sodium ethoxide in benzene to 2-ethoxycarbonyl-1-methyl-3-piperidone (VI; R = H, R′ = CO_2Et), which on acid hydrolysis furnishes 1-methyl-3-piperidone (VI; R = R′ = H); the 3-phenyl ester (V; R = Ph) reacted similarly with sodium hydride, and the product on hydrolysis afforded 1-methyl-4-phenyl-3-piperidone (VI; R = Ph, R′ = H). These 3-piperidones are readily oxidised, even by air at room temperature: they form stable hydrochlorides, but very unstable quaternary salts.

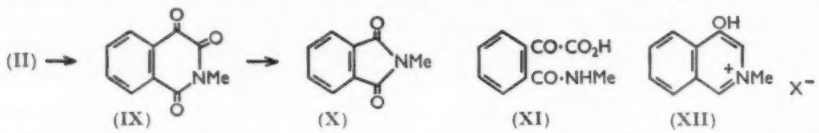
We have similarly condensed ethyl *o*-chloromethylbenzoate with the ethyl ester of sarcosine to give the ethyl ester of *N*-(*o*-ethoxycarbonylbenzyl)sarcosine (VII). The latter, when treated either with sodium ethoxide in boiling benzene or with sodium in boiling xylene, underwent cyclisation to give 3-ethoxycarbonyl-1 : 2 : 3 : 4-tetrahydro-2-methyl-4-oxo*iso*quinoline (VIII), a pale yellow liquid which darkened in air and in



methanol gave a purple colour with ferric chloride. The ester (VIII) in boiling 18% hydrochloric acid underwent hydrolysis and decarboxylation, furnishing the hydrochloride of the tetrahydro-2-methyl-4-oxo*iso*quinoline (II) in 31% yield, based on the *o*-chloromethylbenzoate used. The pure base (II), like the ester (VIII), is also a pale yellow oil which darkens in air: it forms a stable colourless hydrochloride and methiodide, which readily recrystallise. The infrared spectrum of the base (II) shows the $>C{:}O$ band at 1690 and the =NMe band at 2755 cm.$^{-1}$; that of the hydrochloride shows the $>C{:}O$ band at 1692 and the $\equiv NH^+$ band at 2420 cm.$^{-1}$

In view of the novel nature of the keto-amine (II), its reactions with various reagents are now recorded, with the exception of the series of compounds which can be obtained initially by condensation of the keto-amine (II) with *o*-aminobenzaldehyde: these compounds will be described later.

The oxo*iso*quinoline (II), when heated in dichromic–sulphuric acid solution, is oxidised to 1 : 2 : 3 : 4-tetrahydro-2-methyl-1 : 3 : 4-trioxo*iso*quinoline (IX): when air is bubbled through a suspension of the base (II) in aqueous sodium hydroxide even at room temper-



ature, oxidation with ring contraction occurs to form *N*-methylphthalimide (X). It is probable that this oxidation proceeds through the trioxo-compound (IX), for Freund and Beck[8] have shown that 1 : 2 : 3 : 4-tetrahydro-2-methyl*iso*quinoline is also oxidised by dichromic acid to the trioxo-compound (IX), which with alkaline permanganate readily gives the phthalimide (X). Elderfield[9] has suggested that the last stage in this process, namely, (IX) ⟶ (X), involves the intermediate formation of the amide (XI).

The oxo*iso*quinoline (II) in aqueous-alkaline suspension is dehydrogenated at room temperature even by cupric chloride to form the 4-hydroxy-2-methyl*iso*quinolinium cation, isolated as the picrate (XII; X = ·O·$C_6H_2O_6N_3$). Bromine in cold carbon tetrachloride similarly converts the free base (II) into the bromide (XII; X = Br): the use of

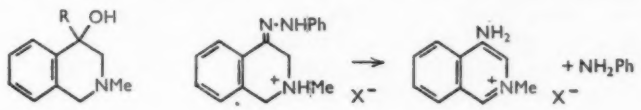
[7] Prill and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 1236; McElvain and Laughton, *ibid.*, 1951, **73**, 448.
[8] Freund and Beck, *Ber.*, 1904, **37**, 1945.
[9] Elderfield, "Heterocyclic Compounds," Wiley, New York, 1952, Vol. IV, p. 405.

an excess of bromine, with subsequent warming, furnished in addition the trioxo-compound (IX) in small yield.

Aqueous bromine, and *N*-bromosuccinimide in carbon tetrachloride, apparently cause complex reactions, and from the products only the hydrobromide of the base (II) has been isolated.

The keto-group in the base (II) behaves normally with lithium aluminium hydride and with phenylmagnesium bromide, giving tetrahydro-4-hydroxy-2-methyl*iso*quinoline (XIII; R = H) and its 4-phenyl derivative (XIII; R = Ph) respectively. The latter on dehydration affords 1 : 2-dihydro-2-methyl-4-phenyl*iso*quinoline.

Condensation of the keto-group in the base (II) with phenylhydrazine and similar compounds reveals a striking reaction. A cold ethanolic solution of the hydrochloride of the base (II), when treated with 1·5 equivalents of phenylhydrazine, slowly deposits the white crystalline phenylhydrazone hydrochloride (XIV; X = Cl): this salt is stable to aerial oxidation and can be readily converted into a number of analogous stable salts. The white free phenylhydrazone can be obtained by the action of aqueous alkali on the hydrochloride in nitrogen: it is, however, highly unstable in the presence of air, forming a red viscous syrup from which no definite product could be isolated. The salts of the phenylhydrazone readily undergo a dismutation to equivalent quantities of the corresponding salt of the 4-amino-2-methyl*iso*quinolinium cation (XV) and aniline. The hydrochloride (XIV; X = Cl), for example, undergoes this change on attempted sublimation, and also rapidly



(XIII) (XIV) (XV)

when heated with ethanolic hydrogen chloride, dilute sulphuric acid, or glacial acetic acid. This ready reaction prevents therefore the successful application of the Fischer indolisation reaction, which requires an acidic medium.

The 2 : 4-dinitrophenylhydrazone and the semicarbazone of the base (II) also give the cation (XV) in the presence of warm acids, and the reaction affords another notable example of the readiness with which the heterocyclic ring in the base (II) and its derivatives undergoes aromatisation.

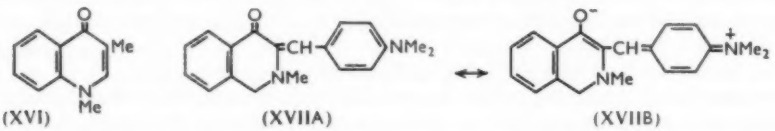
An ethanolic solution of the base (II) containing sodium acetate and a considerable excess of phenylhydrazine, when boiled for one day in air, deposited deep orange crystals, of empirical formula $C_{22}H_{17}N_5$. The infrared spectrum of this product showed the absence of an >NH group. The low solubility made reliable molecular-weight determinations difficult, and its structure has not been elucidated.

The hydrochloride of the base (II) did not react with hydrazine, or undergo the Mannich reaction with dimethylamine and formaldehyde. It is noteworthy that the isomeric base (I) gave the Mannich reaction, but the product spontaneously decomposed to form the 3-methylene derivative, which isomerised to the very stable 1 : 4-dihydro-1 : 3-dimethyl-4-oxoquinoline [10] (XVI): a similar series of reactions, involving an analogous migration of a hydrogen atom, is clearly not possible with the base (II). Furthermore, the base (II), unlike its isomer (I), did not react with malononitrile under the usual conditions,[11] and it did not form a cyanohydrin.

The reactivity of the 3-methylene group in the base (II) is shown by the action of benzaldehyde, which gives an unstable pale yellow 3-benzylidene derivative, and of *p*-dimethylaminobenzaldehyde, which gives the stable orange 3-(*p*-dimethylaminobenzylidene) derivative (XVII). The colour and stability of this compound indicate a contributory

[10] Ittyerah and Mann, *J.*, 1958, 467.
[11] McElvain and Lyle, *J. Amer. Chem. Soc.*, 1950, **72**, 384; Ittyerah and Mann, *J.*, 1956, 3179.

polar form (XVIIB), and this is confirmed by the formation of a colourless diperchlorate: the compound is in fact a *mero*cyanine. The base (II) also reacted with *p*-nitrosodimethylaniline to form a deep red 3-(*p*-dimethylaminophenylimino)-derivative, which was too unstable to allow isolation in the pure state. Spectroscopic examination of the corresponding derivative from the base (I) had shown that a hydrogen atom had migrated from

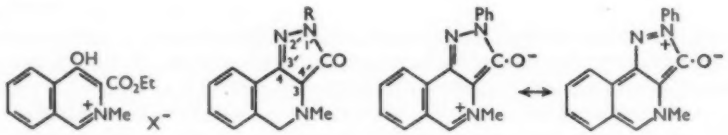


(XVI) (XVIIA) (XVIIB)

the 2-position to the imino-nitrogen atom, and that the compound was therefore the isomeric 3-(*p*-dimethylaminoanilino)-derivative, having the stable heterocyclic ring of the compound (XVI): this stabilising isomeric change is again impossible in our *iso*quinoline analogue.

Attempted condensation of the keto-amine (II) with various diazo-salts in aqueous sodium acetate solution did not succeed.

3-Ethoxycarbonyl-4-oxo*iso*quinoline (VIII) differed from the keto-amine (II) and from tetrahydro-2-methyl*iso*quinoline in that a hot sulphuric–dichromic acid solution oxidised it to *N*-methylphthalimide, and the intermediate trioxo-derivative (IX) was not isolated. It was also very readily dehydrogenated by cold aqueous cupric acetate with the formation of the 3-ethoxycarbonyl-4-hydroxy-2-methyl*iso*quinolinium cation (XVIII), which has been isolated as the perchlorate and picrate and with hot hydrochloric acid readily undergoes hydrolysis and decarboxylation to form the cation (XII), also isolated as the picrate.



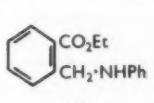
(XVIII) (XIX) (XXA) (XXB)

The 3-ethoxycarbonyl base (VII) in hot ethanolic solution reacted with hydrazine and with phenylhydrazine to give compounds whose analyses indicated the expected pyrazolino*iso*quinolines (XIX; R = H and Ph, respectively): the salts of the last compound also had the expected composition. The structure (XIX) must, however, at present be accepted with reserve. Both hydrazine derivatives are deep red and form pale yellow hydrochlorides, whereas compounds of structure (XIX) should be colourless: both derivatives, moreover, are appreciably soluble in water. If, however, the hydrazine had in each case dehydrogenated the pyrazoline (a process which has been recorded [12]), *mero*cyanines would have been produced, of which (XXA and B) are the two contributory polar forms of the 1′-phenyl derivative, and deep colour would be expected. Chemical analysis does not differentiate decisively between the forms (XIX) and (XXA–B), and the infrared and nuclear magnetic resonance spectra give inconclusive structural evidence.

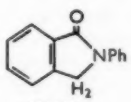
The infrared spectrum of the 1′-phenyl compound in Nujol and in hexachlorobutadiene mulls shows a strong band at 1635 cm.$^{-1}$, which most probably indicates a strong conjugated or amide-type $>C{:}O$ group: it could possibly indicate a $>C{:}N-$ group in a conjugated system but its intensity is rather great for this assignment. The spectrum is virtually unchanged when a chloroform solution is employed. The nuclear magnetic resonance spectrum shows a strong sharp band at 1·10, which could represent a methyl group of the type $Me{\cdot}N^{+}{\equiv}$ or $Me{\cdot}N(-C{=}C-)_2$, but not one of the normal $Me{\cdot}N{=}$ type, which

[13] Gardner, Haynes, and Brandon, *J. Org. Chem.*, 1957, **22**, 1206.

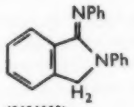
should have $\sigma \sim 2{\cdot}0$—$2{\cdot}5$. The infrared spectrum of the hydrochloride of the 1′-phenyl compound shows a broad band at 2610 cm.$^{-1}$, probably indicating a $\equiv NH^+$ group (although it might indicate a strongly hydrogen-bonded OH group), and a strong band at 1674 cm.$^{-1}$, which suggests a normal conjugated $\rangle C{:}O$ group: the change in position of this band on salt formation is striking. These results do not afford strong support for the structure (XIX) or (XXA–B), or for that expected for their salts.



(XXI)



(XXII)

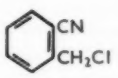


(XXIII)

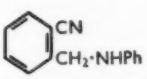
It is noteworthy that the infrared spectrum of the simpler 1 : 3-diphenylpyrazol-5-one in the above mulls shows no $\rangle C{:}O$ absorption, but has a broad band centred at *ca.* 2500 cm.$^{-1}$ which might indicate a $\equiv NH^+$ group or a strongly hydrogen-bonded OH group.

The synthesis of 1 : 2 : 3 : 4-tetrahydro-4-oxo-2-phenyl*iso*quinoline has been briefly investigated. The *N*-phenyl analogue of the *N*-methyl-diester (VII) could not be prepared, for the ethyl ester of *N*-phenylglycine did not condense with ethyl *o*-chloromethyl- or *o*-bromomethyl-benzoate. The alternative intermediate (XXI) could not be prepared by interaction of ethyl *o*-chloromethylbenzoate and aniline (2 equivalents), for these compounds at room temperature readily gave 1-oxo-2-phenyl*iso*indoline (XXII).

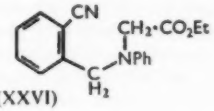
o-Chloromethylbenzonitrile (XXIV) with aniline at 100° in the absence of a solvent gave 2-phenyl-1-phenylimino*iso*indoline (XXIII) in low yield, but in boiling ethanol furnished *N*-2-cyanobenzylaniline (XXV). This compound in turn with ethyl bromoacetate gave the ethyl ester of *N*-2-cyanobenzyl-*N*-phenylglycine (XXVI) but only in very low yield.



(XXIV)



(XXV)



(XXVI)

This nitrile-ester when treated in boiling xylene with sodium gave only a tar, and in boiling ethanol with sodium ethoxide gave 1-oxo-2-phenyl*iso*indoline (XXII). The failure to achieve this cyclisation was not unexpected, as it would have involved a mechanism essentially different from that of the cyclisation of the diester (VII).

Experimental

Consistent m. p.s of certain compounds could be obtained only by the use of evacuated capillary tubes, noted as (E.T.): the temperature of immersion, if above room temperature, is denoted as (T.I.).

Ethyl o-Chloromethylbenzoate.—Chlorine was bubbled through *o*-toluoyl chloride at 185—200° until the increase in weight was 90% (not more!) of that required for monochlorination. Fractional distillation gave *o*-chloromethylbenzoyl chloride, b. p. 135°/14 mm. (lit.,[13] 129—133°/12 mm.), in almost theoretical yield, allowing for recovered *o*-toluoyl chloride, b. p. 108°/14 mm. A solution of the benzoyl chloride in a large excess of ethanol was set aside for 24 hr. and then evaporated under reduced pressure: the residue on distillation gave the chloromethylbenzoate, b. p. 140°/14 mm. (lit.,[13] 139—143°/12 mm.) in almost theoretical yield.

Ethyl *o*-bromomethylbenzoate was prepared by the method of Davies and Perkin;[14] it was used without distillation since when heated it readily gave phthalide. In later experiments it was replaced by the chloro-derivative.

[13] Morgan and Porter, *J.*, 1926, 1262.
[14] Davies and Perkin, *J.*, 1922, **121**, 2207.

XUM

Ethyl Ester of Sarcosine.—Sarcosine nitrile, b. p. 96°/1 mm., was prepared in 70% yield from methylamine hydrochloride by Staudt's method: [15] it gave a picrate, needles, m. p. 147—148° (lit.,[16] 142—143°) from ethanol (Found: C, 38·4; H, 4·1. Calc. for $C_3H_6N_2,C_6H_3O_7N_3$: C, 38·1; H, 4·0%). Its conversion into the ester is much improved as follows: Dry hydrogen chloride was passed slowly into a cold solution of the nitrile (200 g.) in absolute ethanol (2 l.) under reflux, the heat of the reaction eventually boiling the solution, which was then cooled, resaturated with the chloride, and heated under reflux for 8 hr. The cold solution, filtered to remove ammonium chloride, was evaporated under reduced pressure. The crude crushed residual sarcosine ester hydrochloride was added to an excess of liquid ammonia, which was then allowed to evaporate. An ethereal extract of the residue, when dried (Na_2SO_4) and distilled, gave the ester (135 g., 40%), b. p. 46—51°/13 mm. (lit.,[16] 52°/15 mm.). The use of chilled 10% aqueous sodium hydroxide in place of the ammonia gave inconsistent yields, never above 28%.

The base (II) is best prepared and stored as its stable hydrochloride without purification of the intermediate compounds. The isolation and identification of these compounds are briefly noted.

Ethyl Ester of N-(o-*Ethoxycarbonylbenzyl*)*sarcosine* (VII).—A solution of the ethyl ester of sarcosine (109 g., 2 mols.) in ether (100 c.c.) was added slowly to an ice-cooled solution of ethyl *o*-chloromethylbenzoate (92 g., 1 mol.) in ether (100 c.c.) which was then set aside at room temperature for 24 hr. The ether was distilled, and the residue extracted with water (to remove sarcosine ester hydrochloride) and with ether. The ethereal extract was dried (Na_2SO_4), and on evaporation left the diester (VII) (136 g., almost 100%). A sample on distillation gave the pure *diester* (VII), b. p. 182—183°/10 mm. (Found: C, 64·6; H, 8·0; N, 5·3. $C_{15}H_{21}O_4N$ requires C, 64·5; H, 7·5; N, 5·0%). The use of ethyl *o*-bromomethylbenzoate gave a product requiring extensive fractionation.

The diester gave a *chloroplatinate* as a buff powder, m. p. 204·5° (decomp.) (Found: C, 37·6; H, 4·7. $2C_{15}H_{21}O_4N,H_2PtCl_6$ requires C, 37·3; H, 4·4%).

3-*Ethoxycarbonyl*-1 : 2 : 3 : 4-*tetrahydro*-2-*methyl*-4-*oxo*isoquinoline (VIII).—A mixture of the diester (VII) (45 g.), sodium ethoxide (15 g., 1·3 mols.), and benzene (100 c.c.) was heated under a reflux air-condenser carrying a stillhead and receiver, so that an azeotropic ethanol–benzene fraction slowly distilled (*ca.* 4 hr.). The cold mixture was shaken with water, to which concentrated hydrochloric acid was added until the mixture was just acid to Congo Red. An excess of sodium hydrogen carbonate was added, and the benzene layer when dried (Na_2SO_4) and distilled gave the yellow oily *ester* (VIII), b. p. 130°/0·65 mm. (Found: C, 66·0; H, 6·7; N, 6·0%; *M*, in freezing benzene, 210. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·5; N, 6·0%; *M*, 233). It gave a yellow crystalline *picrate*, m. p. 128—129° (from ethanol) (Found: C, 49·6; H, 3·8; N, 12·2. $C_{13}H_{15}O_3N,C_6H_3O_7N_3$ requires C, 49·4; H, 3·9; N, 12·1%), and an orange *chloroplatinate*, m. p. 176—177°, precipitated from an ethanolic solution of the ester (Found: C, 37·7; H, 4·5. $2C_{13}H_{15}O_3N,H_2PtCl_6,2C_2H_6O$ requires C, 37·2; H, 4·6%). Dry hydrogen chloride, when passed into an ethereal solution of the ester, deposited the hygroscopic white hydrochloride, m. p. 137°; an ethanolic solution similarly deposited the white hydrobromide, m. p. 172°.

Tetrahydro-2-*methyl*-4-*oxo*isoquinoline (II).—The undistilled diester (VII) (136 g.), prepared as described above, was added to " molecular " sodium in xylene [sodium (12 g.) and xylene (250 c.c.)], which was vigorously stirred under nitrogen whilst heated under reflux for 8 hr. The cold dark brown product was extracted with dilute hydrochloric acid, which was filtered and treated with sodium hydrogen carbonate in excess, the liberated ester (VIII) being then extracted with ether. The ether was in turn extracted with 18% hydrochloric acid (400 c.c.), which was boiled under reflux for 12 hr., charcoal (1 g.) being added after the first 4 hr. The hot filtered solution was evaporated to dryness under reduced pressure. The brown crystalline residue, when washed with boiling ethanol (2 × 200 c.c.) and dried, afforded the pure colourless *hydrochloride* of the base (II), m. p. 250° (sealed tube) (24 g., 31%) (Found: C, 60·8; H, 6·1; N, 7·0. $C_{10}H_{11}ON,HCl$ requires C, 60·7; H, 6·1; N, 7·1%). The consistently high yields obtained by this method depend largely on the fact that distillation of the intermediate esters (VII) and (VIII) is avoided.

The *base* (II), when liberated from the hydrochloride, extracted with ether, dried, and

[15] Staudt, *Z. physiol. Chem.*, 1925, **146**, 286.
[16] Dalgliesh and Mann, *J.*, 1947, 658.

distilled in nitrogen, formed a pale yellow oil, b. p. 81—83°/0·4 mm. (Found: C, 73·4; H, 6·7; N, 8·6. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·8; N, 8·7%).

Addition of concentrated hydrobromic acid to the ethanolic base precipitated the colourless *hydrobromide*, m. p. 242—244° (decomp.) (from 96% ethanol) (Found: C, 49·7; H, 5·1; N, 5·7. $C_{10}H_{11}ON,HBr$ requires C, 49·6; H, 5·0; N, 5·8%). The colourless *perchlorate*, similarly prepared and recrystallised, had m. p. 159—164° (T.I. 120°) (Found: C, 45·5; H, 4·9; N, 5·4. $C_{10}H_{11}ON,HClO_4$ requires C, 45·9; H, 4·6; N, 5·4%). The base gave a *picrate*, m. p. 133° (decomp., T.I. 127°) (from ethanol) (Found: C, 49·2; H, 3·4; N, 14·7. $C_{10}H_{11}ON,C_6H_3O_7N_3$ requires C, 49·2; H, 3·6; N, 14·3%). This picrate, when subjected to repeated crystallisation from ethanol in the presence of air underwent dehydrogenation, with conversion into *4-hydroxy-2-methylisoquinolinium picrate* (XII; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 227° (see below) (Found: C, 49·5; H, 3·4; N, 14·0. $C_{16}H_{12}O_8N_4$ requires C, 49·5; H, 3·1; N, 14·4%).

A solution of the base (II) in methyl iodide, when boiled for 1 hr. and evaporated, gave the methiodide, m. p. 196—197° (from methanol): this salt gave the yellow crystalline *methopicrate*, m. p. 207—208° (from methanol) (Found: C, 51·1; H, 4·1; N, 14·0. $C_{17}H_{16}O_8N_4$ requires C, 50·9; H, 4·0; N, 13·9%).

Oxidation of the Base (II).—(*A*) Sodium dichromate (2 g.) was added to a solution of the keto-amine hydrochloride (0·5 g.) in water (5 c.c.) and sulphuric acid (18 c.c.), which was then boiled for 30 min., white needles separating meanwhile. The needles, when collected from the cold mixture, washed with water, and dried, afforded tetrahydro-2-methyl-1 : 3 : 4-trioxo*iso*quinoline (IX) (0·35 g., 75%), m. p. 186—188° (lit.,[8] 186—187°) (from ethanol) (Found: C, 63·4; H, 3·5. Calc. for $C_{10}H_7O_3N$: C, 63·5; H, 3·7%).

(*B*) A fine jet of air was blown through the suspension of the base (II) prepared by the addition of the keto-amine hydrochloride (1 g.) in water (5 c.c.) to 10% aqueous sodium hydroxide (50 c.c.). The colour deepened and the suspension slowly formed a dark brown tar. After 45 min., ether (10 c.c.) was added to dissolve much of the tar, and the air-current then deposited a trace of brown powder. The filtered solution was extracted with ether (7 × 250 c.c.), and the extract dried (Na_2SO_4) and evaporated. The residual dark yellow oil, when rubbed in turn with ethanol and light petroleum (b. p. 40—60°), afforded crystalline *N*-methylphthalimide, needles, m. p. 129° (lit.,[8] 133—134°) after sublimation at 130°/0·0001 mm. It was identified by its infrared spectrum, which showed bands at 1755 and 1722 cm.$^{-1}$, characteristic of the phthalimide ring.

Dehydrogenation of the Base (II).—(*A*) 5% Aqueous sodium hydroxide (2 c.c., 1 mol.) was added to a solution of the keto-amine hydrochloride (0·5 g., 1 mol.) and cupric chloride dihydrate (0·85 g., 2 mols.) in water (25 c.c.), which was set aside for 24 hr. The greyish-white precipitate, when recrystallised from dilute hydrochloric acid, gave a chlorocuprite of the cation (XII). This powdered salt, when added to hot aqueous sodium picrate, deposited 4-hydroxy-2-methyl-*iso*quinolinium picrate (XII; X = $C_6H_2O_7N_3$), m. p., mixed and unmixed, 224—228° (E.T.) (from ethanol).

(*B*) Bromine (0·25 g.) in carbon tetrachloride (10 c.c.) was added dropwise with shaking to the free base (0·25 g., 1 mol.) in carbon tetrachloride (10 c.c.). The clear colourless solution was decanted from the precipitated yellowish gum, a solution of which in ethanol was then boiled (charcoal), filtered, cooled, and diluted with ether. The crystalline bromide (XII; X = Br), m. p. 224—230° (E.T.), which separated could not be readily recrystallised and was therefore converted into the picrate (XII; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 222—226° (E.T.).

When an excess of bromine was used and the mixture then evaporated to dryness, the residue when heated at 135°/0·0001 mm. gave a small sublimate of the trioxo*iso*quinoline (IX), m. p. 185—186° (mixed m. p. 184—187°) after crystallisation from ethanol. The unsublimed residue, m. p. 233°, was almost certainly the bromide (XII; X = Br).

N-Bromosuccinimide (0·3 g.) and benzoyl peroxide (trace) were added to a stirred solution of the base (II) (0·25 g.) in carbon tetrachloride (7 c.c.) under nitrogen, giving an immediate yellow precipitate. After 6 hr., the orange deposit was collected and thrice recrystallised from ethanol giving the hydrobromide of the base (II), m. p. 239—240° (decomp.) (E.T., T.I. 195°), mixed m. p. 240—242° (Found: C, 49·4; H, 4·9; N, 5·7%), which gave the picrate of the base, m. p. and mixed m. p. 132—133° (T.I. 120°). The hydrobromide is almost certainly formed by the interaction of the orange solid and the hot solvent.

XUM

Reduction of the Base (II).—An ethereal solution of the base was added to an excess of lithium aluminium hydride in ether, which boiled spontaneously during the addition. The mixture was set aside for 12 hr., the excess of hydride destroyed by dilute sulphuric acid, and the mixture neutralised with sodium carbonate and extracted with ether. Evaporation of the dried extract afforded crude 1 : 2 : 3 : 4-tetrahydro-4-hydroxy-2-methyl*iso*quinoline (XIII; R = H) as a brown oil, which gave a yellow *picrate*, m. p. 149—150° (from ethanol) (Found: C, 49·4; H, 4·6; N, 14·2. $C_{10}H_{13}ON,C_6H_3O_7N_3$ requires C, 49·0; H, 4·1; N, 14·3%).

An ethereal solution of phenylmagnesium bromide was added with stirring to a similar solution of the base (II), under nitrogen. After 15 min., the mixture was hydrolysed with dilute hydrochloric acid, and the aqueous layer separated, neutralised with sodium carbonate, and extracted with ether. Evaporation gave *tetrahydro-4-hydroxy-2-methyl-4-phenylisoquinoline* (XIII; R = Ph), m. p. 107·5—108·5° (from ethanol) (Found: C, 80·2; H, 7·1; N, 5·8. $C_{16}H_{17}ON$ requires C, 80·3; H, 7·2; N, 5·9%). Hydrogen chloride, when passed into an ethanolic solution, gave the colourless *hydrochloride*, m. p. 219° (T.I. 206°) (from ethanol) (Found: C, 69·8; H, 6·6. $C_{16}H_{17}ON,HCl$ requires C, 69·7; H, 6·6%). The yellow *picrate* had m. p. 179° (decomp.) (from ethanol) (Found: C, 56·2; H, 4·1; N, 12·1. $C_{16}H_{17}ON,C_6H_3O_7N_3$ requires C, 56·4; H, 4·3; N, 12·0%).

A solution of this base (XIII; R = Ph) (0·18 g.) in acetic acid (3 c.c.) and 48% hydrobromic acid (1 c.c.) was boiled under reflux for 15 min., concentrated, and treated with aqueous sodium carbonate, the precipitated colourless syrup being extracted with ether. Evaporation of the extract afforded 1 : 2-dihydro-2-methyl-4-phenyl*iso*quinoline as oily crystals, which gave a yellow *picrate*, m. p. 203—204° (T.I. 100°) after repeated crystallisation from ethanol (Found: C, 58·5; H, 3·9. $C_{16}H_{15}N,C_6H_3O_7N_3$ requires C, 58·6; H, 4·0%).

Action of Phenylhydrazine.—The keto-amine hydrochloride (1 g.) and pure phenylhydrazine (0·75 g., 1·5 mol.) were added to cold ethanol (20 c.c.) under nitrogen. The hydrochloride dissolved within 5 min. and the clear solution soon deposited the *phenylhydrazone hydrochloride* (XIV; X = Cl) as very fine white crystals. The mixture was set aside for 48 hr. to increase the size of the crystals (1·5 g., yield almost theoretical), which when collected and recrystallised from ethanol melted at 190° (effervescence), immediately resolidified, and remelted at *ca.* 260° (Found: C, 66·5; H, 6·2; N, 14·4. $C_{16}H_{17}N_3,HCl$ requires C, 66·8; H, 6·3; N, 14·6%).

The above hydrochloride was added under nitrogen to a mixture of 10% aqueous sodium hydroxide and ether, which was shaken for 30 min. The ether layer was dried ($MgSO_4$) and evaporated, and the residue recrystallised four times from ethanol under nitrogen, affording the colourless *phenylhydrazone*, m. p. 110—119° (slow decomp.) (Found: C, 76·2; H, 7·4; N, 16·6. $C_{16}H_{17}N_3$ requires C, 76·5; H, 6·8; N, 16·7%). The phenylhydrazone was also obtained less expeditiously by the action of phenylhydrazine (1 mol.) on the base (II) in boiling ethanol containing sodium acetate, under nitrogen.

The following salts were obtained by precipitation from an ethanolic solution of the hydrochloride: *picrate* (XIV; X = $C_6H_2O_7N_3$), yellow, m. p. 173° (decomp.) (T.I. 170°) (from ethanol) (Found: C, 54·7; H, 4·7; N, 17·7. $C_{16}H_{17}N_3,C_6H_3O_7N_3$ requires C, 54·7; H, 4·7; N, 17·7%); *perchlorate* (XIV; X = ClO_4), colourless, m. p. 164° (from ethanol) (Found: C, 54·5; H, 4·9; N, 12·2. $C_{16}H_{17}N_3,HClO_4$ requires C, 54·6; H, 5·2; N, 12·0%); *chloroplatinate*, purple-brown, m. p. 164° (decomp.) after thorough washing with ethanol and drying at room temperature (Found: C, 42·7; H, 4·2; N, 9·6. $2C_{16}H_{17}N_3,H_2PtCl_6$ requires C, 42·1; H, 4·0; N, 9·2%).

A solution of the hydrochloride (5 g.) of the base (II), phenylhydrazine (10 g., 2·5 mol.) and sodium acetate (10 g.) in ethanol (50 c.c.) was boiled under reflux in air for 24 hr. and cooled. The solid deposit, when washed with water and ether, gave an orange residue (1·1 g.), which after two recrystallisations from ethanol (in which it was very slightly soluble) afforded orange needles, m. p. 213° (Found, in independent preparations: C, 75·2, 75·1, 75·4; H, 5·1, 5·1, 5·0; N, 20·1, 19·8, 20·1%; *M*, in boiling CCl_4, 300. $C_{22}H_{17}N_5$ requires C, 75·2; H, 4·9; N, 19·9%; *M*, 351). This compound was not obtained when the boiling was conducted in nitrogen.

Action of Acids on the Phenylhydrazone Hydrochloride (XIV; X = Cl).—(i) A solution of the hydrochloride in saturated ethanolic hydrogen chloride, when boiled under reflux for 2 hr. and cooled, deposited crude crystalline 4-amino-2-methyl*iso*quinolinium chloride (XV; X = Cl), which was converted into the yellow *picrate*, m. p. 220—221° (alone and mixed with the

synthetic material described below) (from ethanol) (Found: C, 49·0; H, 3·6; N, 17·5. $C_{16}H_{13}O_7N_5$ requires C, 49·6; H, 3·4; N, 18·1%). The original reaction liquor was basified and extracted with ether, which when separated and evaporated afforded aniline, identified by (*a*) the purple coloration with sodium hypochlorite solution, (*b*) conversion into acetanilide, m. p. and mixed m. p. 110—114°.

(ii) The solution in a similar experiment in which 10% aqueous sulphuric acid was used deposited on cooling colourless needles of the *hydrogen sulphate* (XV; X = HSO_4), m. p. 225—227° after crystallisation from 97% ethanol (Found: C, 47·1; N, 5·0; N, 11·0. $C_{10}H_{12}O_4N_2S$ requires C, 46·9; H, 4·7; N, 10·9%). This salt also gave the picrate, m. p. and mixed m. p. 220—221°. The hydrogen sulphate, when warmed with sodium dichromate in 10% sulphuric acid, readily gave the trioxo-derivative (IX), m. p. and mixed m. p. 185—187° (from ethanol).

(iii) A solution of the hydrochloride in glacial acetic acid, when similarly boiled and then evaporated, gave colourless crystals, presumably the acetate (XV; X = $C_2H_3O_2$), which in turn afforded the picrate, m. p. and mixed m. p. 219—220°, and the hydrogen sulphate, m. p. and mixed m. p. 225—227°.

The hydrochloride (XIV; X = Cl), when heated at 180—190°/0·0001 mm., gave a yellow sublimate, m. p. *ca.* 205° (probably aniline hydrochloride). The residue, dissolved in ethanol, gave the picrate, m. p. and mixed m. p. 220—221°. The hydrochloride (XIV; X = Cl) charred extensively when heated with zinc chloride.

Synthesis of the Picrate (XV; X = $C_6H_2O_7N_3$).—Pure *iso*quinoline was converted by bromine in hydrobromic acid [17] into 4-bromo*iso*quinoline, b. p. 149°/13 mm., which with ammonia and copper sulphate [18] gave 4-amino*iso*quinoline, m. p. 106—108° (lit.,[18] 108·5°) from benzene. A solution of the 4-amino-compound in methanolic methyl iodide, when boiled under reflux for 5 min. and cooled, deposited 4-amino-2-methyl*iso*quinolinium iodide (XV; X = I) as a yellow powder, which was converted into the picrate (XV; X = $C_6H_2O_7N_3$), yellow needles, m. p. 219—221° (from ethanol). This sample was used for mixed m. p. purposes. A methanolic solution of the iodide when treated with perchloric acid deposited the *perchlorate* (XV; X = ClO_4), pale yellow, m. p. 183—184° (E.T.) (from ethanol) (Found: C, 46·6; H, 4·8; N, 10·9. $C_{10}H_{11}O_4N_2Cl$ requires C, 46·4; H, 4·3; N, 10·8%).

A mixture of the keto-amine hydrochloride (3·2 g.) and *N*-methyl-*N*-phenylhydrazine (2·0 g.) in ethanol (20 c.c.) was shaken under nitrogen for 6 hr. A trace of yellow silky crystals was collected, and the dark green filtrate diluted with ether, precipitating a yellow powder, m. p. 285° (decomp.) (T.I. 240°) (from ethanol–ether). This powder, treated with ethanolic sodium picrate, gave the picrate (XV; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 219—222° (T.I. 210°) (Found: C, 50·0; H, 3·9; N, 17·9%), and with perchloric acid gave the perchlorate (XV; X = ClO_4), m. p. and mixed m. p. 184° (E.T.) (Found: C, 46·3; H, 4·2; N, 10·7%).

A similar experiment using *N*-ethyl-*N*-phenylhydrazine gave indefinite results, but the yellow oil left after removal of unchanged reagents at 200°/0·001 mm. gave with ethanolic picric acid the picrate (XV; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 219° (Found: C, 49·9; H, 3·3; N, 18·0%).

A suspension of the keto-amine hydrochloride (1 g.) and powdered 2 : 4-dinitrophenylhydrazine (1 g.) in ethanol (20 c.c.) was shaken under nitrogen for 8 hr., an orange solid slowly separating. The reaction was incomplete after 5 days, so the mixture was warmed for 10 min., then cooled, and the orange crystalline insoluble *dinitrophenylhydrazone* (1 g.), m. p. 213° (decomp.) (T.I. 205°), was collected (Found: C, 54·6; H, 4·6; N, 20·5. $C_{16}H_{16}O_4N_5$ requires C, 56·3; H, 4·4; N, 20·5%. Low and inconsistent carbon values were obtained). A suspension in ethanolic hydrogen chloride was boiled for 90 min., then cooled, and the chloride (XV; X = Cl) was precipitated by ether. It was converted into the picrate (XV; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 219—222°.

A solution of the keto-amine (0·2 g.) in ethanol (1 c.c.) was added to a solution of semicarbazide hydrochloride (0·2 g.) and anhydrous sodium acetate (0·2 g.) in water (1 c.c.), which was boiled for 15 min. Cooling deposited the colourless *semicarbazone*, m. p. 207—209° (from ethanol) (Found: C, 60·4; H, 6·9; N, 25·7. $C_{11}H_{14}ON_4$ requires C, 60·5; H, 6·5; N, 25·7%). A solution of this in ethanolic hydrogen chloride was boiled under reflux for 40 min., and then afforded as before the picrate (XV; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 218—221° (T.I. 215°).

[17] Bergstrom and Rodda, *J. Amer. Chem. Soc.*, 1940, **62**, 3030.
[18] Craig and Cass, *ibid.*, 1942, **64**, 783.

XUM

3-Benzylidene-1 : 2 : 3 : 4-tetrahydro-2-methyl-4-oxoisoquinoline (*as* XVII).—A mixture of the base (II) (0·5 g.), benzaldehyde (0·3 g., 1 mol.), 10% aqueous sodium hydroxide (1·3 c.c.), and ethanol (0·6 c.c.) was thoroughly shaken under nitrogen and set aside for 16 hr., a red oil slowly separating and forming a yellow solid. The mixture was dissolved in a minimum of ethanol, and the *benzylidene derivative* reprecipitated by the addition of water: recrystallisation from aqueous ethanol (*ca.* 1 : 1) gave pale yellow needles (0·5 g., 60%) (Found: C, 81·6; H, 6·3; N, 5·9. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·1; N, 5·6%). The compound slowly decomposed on exposure to air, with liberation of benzaldehyde. It gave a *picrate*, pale yellow plates, m. p. 197° from ethanol (Found: C, 57·7; H, 4·0; N, 12·1. $C_{17}H_{15}ON,C_6H_3O_7N_3$ requires C, 57·7; H, 3·8; N, 11·7%). The white hydrochloride, m. p. 210°, was precipitated when hydrogen chloride was passed into an ethereal solution of the benzylidene derivative.

The 3-p-*dimethylaminobenzylidene derivative* (XVII A–B) was similarly prepared, the mixture being set aside under nitrogen for 5 days. The orange-red crystalline deposit was then increased by cautious addition of water, and when collected and crystallised from aqueous ethanol (9 : 1 by vol.) gave orange crystals, m. p. 125—132° (Found: C, 77·7; H, 6·7; N, 9·8. $C_{19}H_{20}ON_2$ requires C, 78·0; H, 6·9; N, 9·6%). The cautious addition of aqueous-ethanolic perchloric acid to an ethanolic solution until the latter became colourless, followed by the addition of ether, precipitated the *diperchlorate*, colourless needles from ethanol (Found: C, 46·3; H, 4·9; N, 5·9. $C_{19}H_{20}ON_2,2HClO_4$ requires C, 46·3; H, 4·5; N, 5·7%). The colourless hydrochloride, similarly prepared, was too highly deliquescent for ready purification.

The 3-*p*-dimethylaminophenylimino-derivative was similarly prepared by using *p*-nitrosodimethylaniline, with ice-cooling during the mixing: after 1 day, the red crystals were collected but rapidly decomposed.

Reactions of the 3-Ethoxycarbonyl Compound (VIII).—*Oxidation.* This was carried out with sulphuric acid–sodium dichromate, as that of the keto-amine (II), and afforded *N*-methylphthalimide (X), identified as before.

Dehydrogenation. The base (VIII) was added dropwise to a vigorously shaken, cold, saturated aqueous solution of cupric acetate. A white powder was precipitated, and the blue colour, which had faded, was just restored by addition of more acetate solution. The filtered solution was divided into three portions. (i) Cautious addition of 60% perchloric acid diluted with a small quantity of ethanol precipitated the colourless *perchlorate* (XVIII; X = ClO_4), m. p. 157—158° after crystallisation from ethanol (Found: C, 47·0; H, 4·4; N, 4·1. $C_{12}H_{14}O_7NCl$ requires C, 47·1; H, 4·3; N, 4·2%). (ii) The addition of ethanolic picric acid gave the *picrate* (XVIII; X = $C_6H_2O_7N_3$), m. p. 172° after repeated crystallisation from ethanol (Found: C, 49·6; H, 3·8; N, 12·4. $C_{18}H_{16}O_{10}N_4$ requires C, 49·6; H, 3·5; N, 12·2%). (iii) The solution, mixed with 18% hydrochloric acid, was boiled under reflux for 8 hr. and evaporated to dryness: the residue, treated with sodium picrate, both in aqueous solution, deposited the picrate (XII; X = $C_6H_2O_7N_3$), m. p. and mixed m. p. 227° (E.T.) (from ethanol) (Found: C, 50·1; H, 3·7; N, 14·1%).

Reaction with hydrazine and phenylhydrazine. For clarity, the names of these compounds are based on the structure (XIX); in the analytical results, the theoretical values are given for this structure and then for the structure (XX A–B).

A solution of the base (VIII) (1 g.) and 65% aqueous hydrazine (2 c.c., 8 mol.) in ethanol (10 c.c.) was heated under reflux for 30 min., and the red solution cooled and diluted with ether, which precipitated the red *1 : 2 : 3 : 4-tetrahydro-2-methyl-5′-oxopyrazolino(4′ : 3′-3 : 4)isoquinoline* (XIX; R = H), m. p. 290° (slight preliminary decomp.) after three such reprecipitations (Found: C, 65·3; H, 5·0; N, 21·2. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9. $C_{11}H_9ON_3$ requires C, 66·3; H, 4·5; N, 21·1%). An ethanolic solution when treated with dry hydrogen chloride deposited the pale yellow hydrochloride, m. p. 266° (becoming red) (from ethanol).

A similar experiment, with phenylhydrazine (10 mol.) and heating for 4 hr., gave by ethereal precipitation the deep red *1′-phenyl derivative* (XIX; R = Ph), m. p. 234° (from ethanol) (Found: C, 73·95; H, 5·3; N, 15·2. $C_{17}H_{15}ON_3$ requires C, 73·6; H, 5·5; N, 15·2. $C_{17}H_{13}ON_3$ requires C, 74·2; H, 4·8; N, 15·3%). The *hydrochloride*, prepared as above, formed fine yellow needles, m. p. 231° (E.T.) after crystallisation from ethanol containing hydrogen chloride (Found: C, 64·9; H, 4·7; N, 13·4. $C_{17}H_{15}ON_3,HCl$ requires C, 65·1; H, 5·1; N, 13·4. $C_{17}H_{13}ON_3,HCl$ requires C, 65·5; H, 4·5; N, 13·5%). The yellow *picrate*, twice recrystallised from a very dilute picric acid solution in ethanol, had m. p. 229° (Found: C, 55·4; H, 3·5; N,

XUM

17·1. $C_{17}H_{15}ON_3,C_6H_3O_7N_3$ requires C, 54·5; H, 3·6; N, 16·6. $C_{17}H_{13}ON_3,C_6H_3O_7N_3$ requires C, 54·8; H, 3·2; N, 16·7%). A solution of the pyrazolone in methyl iodide was boiled under reflux for 4 hr. and allowed to evaporate. The yellow crystalline residue afforded the *methiodide*, having m. p. 245° (decomp. from 233°) after two crystallisations from methanol (Found: C, 50·9; H, 4·0; N, 9·7. $C_{18}H_{18}ON_3I$ requires C, 51·6; H, 4·3; N, 10·0. $C_{18}H_{16}ON_3I$ requires C, 51·8; H, 3·9; N, 10·1%).

The use of a smaller proportion of hydrazine and of phenylhydrazine (*e.g.*, 2—3 mols.) in the above experiments gave crude products from which crystalline derivatives could not be isolated.

1 : 3-*Diphenylpyrazol-5-one*.—The product obtained by interaction of phenylhydrazine and ethyl benzoylacetate (1 mol.) on gentle warming was poured into ether, and the precipitated solid pyrazolone was triturated with ether, collected, and recrystallised from ethanol; it had m. p. 135—138° (lit.,[19] 137°) (Found: C, 76·2; H, 5·0; N, 12·1. Calc. for $C_{15}H_{12}ON_2$: C, 76·2; H, 5·1; N, 11·9%).

Ethyl o-*Chloromethylbenzoate and Aniline*.—The benzoate (7 g.) and aniline (7 g., 2 mol.), when mixed at room temperature, gave a crystalline deposit within 30 min. After 5 hr. the deposit was extracted with ether, leaving aniline hydrochloride (1·45 g.), m. p. 190°. Evaporation of the ethereal extract afforded a residue which when washed with ether (5 c.c.) gave the crystalline 1-oxo-2-phenyl*iso*indoline (XXII), m. p. and mixed m. p. 158—161°.

o-*Chloromethylbenzonitrile and Aniline*.—(*A*) A mixture of the nitrile, m. p. 54·5° (6 g.), and aniline (14 g., 4 mol.) was heated on a steam-bath for 1 hr., and the black product cooled in ice and neutralised with 10% aqueous sodium hydroxide, giving a black oil under the clear aqueous solution which was then decanted. The oil, when repeatedly shaken with water (2—3 l.), formed a brown solid, which after several recrystallisations from ethanol (charcoal) gave 2-phenyl-2-phenylimino*iso*indoline (XXIII), needles, m. p. 123—130° from room temperature, 150—153° (E.T.) (Found: C, 84·6; H, 6·0; N, 10·0. Calc. for $C_{20}H_{16}N_2$: C, 84·5; H, 5·7; N, 9·9%). An ethereal solution, treated with hydrogen chloride, gave the hydrochloride, m. p. 237—239° (lit.,[20] 237—238°).

(*B*) A solution of the nitrile (45 g.) and aniline (45 c.c., 1·5 mol.) in ethanol (185 c.c.) was heated under reflux for 1 hr., cooled, and poured into ether (1800 c.c.), precipitating the crude hydrochloride (62 g.) of the nitrile (XXV). A solution of this salt in water (500 c.c.), treated with 10% aqueous sodium hydroxide (1 mol.), deposited *N*-2-cyanobenzylaniline (XXV), (48 g., 75%), m. p. 114—121°.

Ethyl Ester of N-2-*Cyanobenzyl*-N-*phenylglycine* (XXVI).—A mixture of the crude nitrile (XXV) (60 g.) and ethyl bromoacetate (70 g., 1·3 mol.) was heated on a steam-bath for 30 min., ethanol (30 c.c.) being added after the first 10 min. The cold solution was poured into ether (2 l.), and the solution decanted from the precipitated black gum. A solution of the gum in water (2·5 l.), after being vigorously shaken (charcoal), gave a pink filtrate, which when treated with 10% aqueous sodium hydroxide (120 c.c.) deposited an oil which solidified. Repeated recrystallisation from 50% aqueous ethanol gave the *ethyl ester* (XXVI) (2·5 g.), m. p. 114·5—115·5° (Found: C, 73·3; H, 6·0; N, 9·6. $C_{18}H_{18}O_2N_2$ requires C, 73·5; H, 6·2; N, 9·5%). It gave a *perchlorate*, m. p. 132—134° (from ethanol) (Found: C, 54·6; H, 4·7; N, 7·2. $C_{18}H_{18}O_2N_2,HClO_4$ requires C, 54·8; H, 4·8; N, 7·1%), and a *picrate*, yellow needles, m. p. 167—170° (from ethanol) (Found: C, 55·1; H, 4·4; N, 13·5. $C_{18}H_{18}O_2N_2,C_6H_3O_7N_3$ requires C, 55·1; H, 4·0; N, 13·4%).

The mother-liquors from the recrystallisation of the ester (XXVI) were concentrated and cooled, giving a second crystalline crop (15 g.) which was recrystallised from 50% aqueous ethanol until the m. p. 101—110° (E.T.) was unchanged. The powdered material was extracted with cold dilute sulphuric acid, and the insoluble residue, when recrystallised as before, gave the *iso*indoline (XXII), m. p. and mixed m. p. 160—165° (E.T.).

Attempted Cyclisation.—The pure ester (XXVI) (0·5 g.) was added to a cold solution of sodium ethoxide prepared from sodium (0·5 g.) and ethanol (10 c.c.), which was then heated under reflux in nitrogen for 4 hr., cooled, poured into water (150 c.c.), and set aside overnight. The precipitated solid when collected and recrystallised from ethanol gave the *iso*indoline (XXII) (0·13 g.), plates, m. p. and mixed m. p. 160—166° (E.T.).

Dropwise addition of bromine water to an ethanolic solution of the ester (XXVI), followed

[19] Knorr and Klotz, *Ber.*, 1887, **20**, 2546.
[20] Thiele and Schneider, *Annalen*, 1909, **369**, 297.

by considerable dilution with dilute aqueous sodium carbonate, gave a crystalline *monobromo-derivative*, m. p. 157—159° (E.T.), shrinking at 145° (Found: C, 57·4; H, 4·7; N, 7·6. $C_{18}H_{17}O_2N_2Br$ requires C, 57·9; H, 4·6; N, 7·5%).

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 29th*, 1958.]

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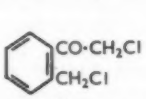
122. *The Interaction of* o-*Chloromethylphenacyl Chloride and Primary Amines: a Novel Formation of the* iso*Indoline System.*

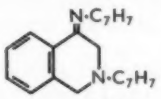
By I. G. HINTON, FREDERICK G. MANN, and A. VANTERPOOL.

o-Chloromethylphenacyl chloride has been prepared by the action of diazomethane on *o*-chloromethylbenzoyl chloride, in order that, by reaction with aniline, it might afford 1 : 2 : 3 : 4-tetrahydro-4-oxo-2-phenyl*iso*quinoline. It condenses, however, with aniline in neutral or weakly basic solution to give 3-methyl-2-phenyl-1-phenylimino*iso*indoline. The *m*-tolyl and *p*-tolyl analogues have been similarly prepared.

BEFORE our successful synthesis of 2-substituted 1 : 2 : 3 : 4-tetrahydro-4-oxo*iso*quinolines,[1] another route was investigated with unexpected results. For this synthesis, we first prepared the crystalline *o*-chloromethylphenacyl chloride (I) by the interaction of *o*-chloromethylbenzoyl chloride and diazomethane. The structure of the chloride (I) has been confirmed by analysis, by the close similarity of its infrared spectrum, particularly in the region 2500—1550 cm.$^{-1}$, with that of phenacyl bromide, and by its nuclear magnetic resonance spectrum which shows the presence of two $>CH_2$ groups. The dibromo-analogue of the compound (I) has also been prepared, but is too unstable for synthetic use.



(I)



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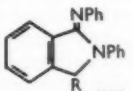


(III)

The interaction of the chloride (I) and *p*-toluidine in boiling ethanol containing potassium carbonate gave a highly crystalline compound of molecular formula $C_{23}H_{22}N_2$, which appeared to be the 4-*p*-tolylimino-derivative (II) of the required tetrahydro-4-oxo-2-*p*-tolyl*iso*quinoline; this structure received support from the absence of a =NH band in the infrared spectrum and the presence of a strong band at 1642 cm.$^{-1}$ indicating a conjugated $>C{=}N-$ group.

The marked stability of this compound, in particular its resistance to acid-hydrolysis and to reduction, did not however accord with structure (II).

We have now prepared the crystalline phenyl and *m*-tolyl analogues of this compound. The phenyl compound is formed slowly by the interaction of the chloride (I) and aniline in cold ethanol, and more rapidly if the solution is boiled, particularly with the addition of potassium carbonate or triethylamine.

The phenyl compound gave a reasonably stable hydrochloride, the infrared spectrum of which indicated a $\equiv NH^+$ group. The base was virtually unaffected by hot dilute hydrochloric or sulphuric acid, by boiling 40% aqueous formaldehyde alone or with hydrochloric acid, and by nitrous acid in cold hydrochloric acid. It gave acetanilide with boiling acetic acid–acetic anhydride, and *N*-phenylphthalimide with sodium dichromate in hot dilute sulphuric acid.

[1] Hinton and Mann, preceding paper.

The infrared absorption of the phenyl compound in carbon tetrachloride solution was closely similar to that of the *p*-tolyl analogue in Nujol and in hexachlorobutadiene, and confirmed the absence of an =NH group. The nuclear magnetic resonance spectrum of the phenyl compound in chloroform solution showed two equal resonance peaks at 3·75 and 3·95 chemical shift units, due to the hydrogen atoms in a methyl group interacting with a single adjacent hydrogen atom. There were also four peaks at −0·2, −0·05, 0·12, and 0·27 unit, approximately in the ratio 1 : 3 : 3 : 1, which is the characteristic pattern given by a single hydrogen atom next to a methyl group. This provides strong evidence for the presence of an Me·CH= group, and, combined with the oxidative formation of *N*-phenylphthalimide, indicates that the compound formed by the interaction of the chloride (I) and aniline is 3-methyl-2-phenyl-1-phenylimino*iso*indoline (III; R = Me).

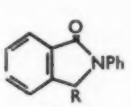
This identification is confirmed by the close similarity of the infrared spectra of authentic 2-phenyl-1-phenylimino*iso*indoline (III; R = H) and our phenyl compound, and of their

Ultraviolet spectra of the iso*indoline* (III; R = H) *and the "phenyl compound"* (III; R = Me) *in* (A) *ethanolic solution,* (B) *this solution diluted with concentrated hydrochloric acid* (1 *drop*) (λ *in* mμ).

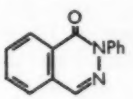
		(A)					(B)			
(III; R = H)	$\lambda_{max.}$	283	236	$\lambda_{min.}$	261	220	$\lambda_{max.}$	246	$\lambda_{min.}$	229
	ε	10,030	24,400	ε	6720	18,830	ε	15,500	ε	11,140
(III; R = Me)	$\lambda_{max.}$	282	235	$\lambda_{min.}$	261	220	$\lambda_{max.}$	246	$\lambda_{min.}$	228
	ε	9300	22,900	ε	7570	18,000	ε	16,280	ε	10,720

ultraviolet absorption spectra (and that of the *p*-tolyl compound) in ethanol and in ethanol–hydrochloric acid. Furthermore, condensation of 3-methyl-1-oxo-2-phenyl*iso*indoline (IV; R = Me) and aniline in phosphorus oxychloride gave the 3-phenylimino-compound (III; R = Me) identical with our product.

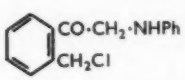
The *iso*indoline (III; R = Me) is of course an amidine, which explains its high stability, particularly towards acid hydrolysis and reduction.



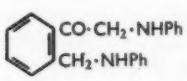
(IV)



(V)



(VI)



(VII)

The formation of the *iso*indoline ring by the action of primary amines on the chloride (I) is surprising: there are many examples of benzene derivatives with two appropriate *ortho*-substituents reacting with amines to give the *iso*indoline ring under conditions which must require either a preliminary tautomeric change of the benzene derivative or a more fundamental molecular rearrangement, but apparently none is known in which a methylene group is extruded as a methyl substituent during the reaction. As examples of the former type, Thiele and Schneider [2] have shown that phthalaldehyde in cold ether reacts with one and two equivalents of aniline to form 1-oxo-2-phenyl*iso*indoline (IV; R = H) and 2-phenyl-1-phenylamino*iso*indoline (III; R = H) respectively. The 1-oxocompound (IV; R = H) is also reported [3] to be formed by the interaction of phthalaldehyde and an excess of aniline at 200—220°, and by the reduction of the compound $C_{14}H_{10}ON_2$, presumably (V), obtained by the interaction of phenylhydrazine and phthalaldehydic acid.[4]

It is known that phenacyl derivatives of aromatic primary amines, Ph·CO·CH_2·NHR, can undergo rearrangement involving an interchange of the phenyl group and a hydrogen atom (or its substituent) of the methylene group,[5] but this reaction is dependent on an

[2] Thiele and Schneider, *Annalen*, 1909, **369**, 297.
[3] Hessert, *Ber.*, 1877, **10**, 1445.
[4] Racine, *Annalen*, 1887, **239**, 78.
[5] Brown and Mann, *J.*, 1948, 847, 858; cf. also Crowther, Mann, and Purdie, *J.*, 1943, 58.

acid catalyst, and our condensations have occurred in neutral or mildly alkaline conditions; moreover, the *iso*indoline (III; R = Me) could not be obtained by interaction of the chloride (I) and aniline hydrobromide. The phenacylamine rearrangement, even if it occurred with either of the possible intermediates (VI) and (VII), offers no reasonable mechanism for the formation of *iso*indoline (III; R = Me), and the actual mechanism awaits further investigation.

Experimental

All compounds, unless otherwise stated, were colourless. M. p.s when determined in evacuated tubes are denoted as (E.T.), and temperature of immersion as (T.I.).

The successful preparation of the chloride (I) depends on the rigid adherence to certain conditions specified below: in particular, all apparatus must be carefully dried and closed with drying-tubes during use.

o-*Chloromethylbenzoyl Chloride*.—*o*-Toluoyl chloride, b. p. 212°, was prepared in 94% yield by the interaction of the acid and thionyl chloride.[6] The chloride (48·7 g.), in a weighed flask fitted with an inlet tube and a reflux air-condenser carrying a drying tube, was heated to 170—180° while chlorine was passed through. When the increase in weight indicated 90% monochlorination, the mixture was fractionally distilled, giving *o*-chloromethylbenzoyl chloride (48·6 g., 81%), b. p. 87·5—88·5°/0·5 mm. (lit.,[7] 129—133°/12 mm.). In this fractionation, unchanged *o*-toluoyl chloride can readily be separated; but, if full monochlorination is attempted, the chloromethyl derivative becomes contaminated with the dichloromethyl compound, having almost the same b. p.

A solution of the chloride (6·6 g.) in 98% formic acid [8] (50 c.c.) was shaken at room temperature for 75 min. The addition of water (200 c.c.) then precipitated *o-chloromethylbenzoic acid* (5·8 g., 98%), white plates, m. p. 135—135·5° (Found: C, 56·45; H, 4·3. $C_8H_7O_2Cl$ requires C, 56·3; H, 4·1%).

o-*Chloromethylphenacyl Chloride* (I).—The ethereal diazomethane must be free from ethanol, and it was therefore prepared by the action of aqueous potassium hydroxide on methylnitrosourea, in preference to that of aqueous-ethanolic potassium hydroxide on *N*-methyl-*N*-nitrosotoluene-*p*-sulphonamide.

A 2·1% (w/v) solution of diazomethane in ether was thoroughly dried over powdered potassium hydroxide in an ice–salt bath. The solution (330 c.c., 1 mol. of reagent) was filtered rapidly into a nitrogen-filled flask, carrying a dropping-funnel and stirrer, cooled in ice–salt. A solution of triethylamine (16 g., 1 mol.) in ether (20 c.c.) was added to the vigorously stirred solution, followed by *o*-chloromethylbenzoyl chloride (30 g., 1 mol.) in ether (100 c.c.) during 15 min. The stirring was continued for 30 min. and the mixture set aside at room temperature overnight.

The solution was rapidly filtered from triethylamine hydrochloride, and transferred immediately to a 3-necked flask having a thermometer dipping below the surface, and a fine inlet tube reaching to the bottom. The solution was cooled to −2° in ice–salt, and dry hydrogen chloride then passed slowly in, the temperature being kept below 5° meanwhile. The initial precipitate slowly redissolved to give a brown solution, which, when the nitrogen evolution ceased (*ca.* 1½ hr.), was evaporated under reduced pressure at 40°. The residual brown oil was dissolved in methanol (3 × 10 c.c.), and the solution when cooled and stirred deposited the crude chloride (I). Addition of water to the mother-liquor deposited further crops (total, 64%), and recrystallisation from methanol gave the *chloride* (I), colourless needles, m. p. 41—42° (Found: for independent preparations, C, 53·4, 53·3; H, 4·2, 4·1. $C_9H_8OCl_2$ requires C, 53·2; H, 4·0%).

In early experiments, in which 100% monochlorination of the *o*-toluoyl chloride was attempted, the mother-liquors when distilled in steam gave a brown solid which after repeated recrystallisation from aqueous ethanol afforded *o-dichloromethylphenacyl chloride*, needles, m. p. 57·5—58° (Found: C, 45·3; H, 3·0. $C_9H_7OCl_3$ requires C, 45·5; H, 3·0%).

The pure dry chloride (I) can be safely stored for months in a dark refrigerator. It must be handled with care for it is a skin-irritant and a lachrymator.

[6] Davies and Perkin, *J.*, 1922, **121**, 2202.
[7] Morgan and Porter, *J.*, 1926, 1256.
[8] Shoesmith, Hetherington, and Slater, *J.*, 1924, **135**, 1312.

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o-*Bromomethylphenacyl Bromide.*—*o*-Bromomethylbenzoyl bromide, white needles, m. p. 36° (lit.,[6] 33—34°), was obtained in 63% yield by the action of bromine on *o*-toluoyl chloride. The reaction with diazomethane was carried out as before, the solution being now treated with hydrogen bromide. The filtered solution was washed in turn with water, 5% aqueous sodium hydrogen carbonate, and water, and finally dried (Na_2SO_4) and cautiously evaporated under reduced pressure. The brown crystalline residue (54%) when recrystallised (charcoal) from methanol, *cyclo*hexane, or light petroleum (b. p. 40—60°) gave the *bromide*, needles, m. p. 55·5—56° (decomp.) (Found: C, 37·3; H, 2·8; Br, 55·5. $C_9H_8OBr_2$ requires C, 37·0; H, 2·8; Br, 54·7%). The bromide decomposed when stored in an evacuated desiccator in the dark for 12 days. Several samples of the crude bromide whilst being dried in a desiccator decomposed violently when almost free from solvent, and the preparation demands safety precautions.

3-*Methyl*-2-*phenyl*-1-*phenylimino*isoindoline (III; R = Me).—A mixture of the chloride (I) (2·4 g.), aniline (4 g., 4 mols.), dry potassium carbonate (1·6 g.), and ethanol (20 c.c.) was boiled under reflux for 1 hr., cooled, and poured on ice (200 g.). The crude pale brown iso*indoline* (III; R = Me) (3·2 g., 89%) after several recrystallisations from ethanol gave colourless needles, m. p. 149—151° (E.T.) (Found: C, 84·4; H, 6·2; N, 9·6. $C_{21}H_{18}N_2$ requires C, 84·5; H, 6·1; N, 9·4%).

A solution of the chloride (I) and aniline (2 mols.) in ethanol, when boiled under reflux for 1 hr., cooled, and poured into water, gave a clear solution from which the addition of 10% aqueous sodium hydroxide immediately precipitated the *iso*indoline (III), m. p. 146·5—149° after one recrystallisation from ethanol. Repetition of this experiment with aniline hydrobromide (2 mols.) gave on precipitation a purple oil which could not be obtained solid. A solution of the chloride (I) (0·4 g.) and aniline (1 g., 5 mols.) in ethanol (10 c.c.) was prepared under nitrogen at 0° and set aside overnight at room temperature. The pale brown solution when poured into aqueous sodium carbonate deposited the oily *iso*indoline (III), which when stirred with cold ethanol afforded white crystals, m. p. and mixed m. p. 140—148° (E.T.) without recrystallisation.

Hydrogen chloride, when passed into an acetone–ethanol solution of the *iso*indoline (III), precipitated a brown gum, which when vigorously stirred with ether formed the *hydrochloride* as a white powder, m. p. 205° (darkening from 190°) after drying at 70°/0·1 mm. (Found: C, 75·1; H, 5·5; N, 8·2. $C_{21}H_{18}N_2$,HCl requires C, 75·4; H, 5·7; N, 8·4%).

3-*Methyl*-2-p-*tolyl*-1-p-*tolylimino*isoindoline (as III; R = Me).—This compound was prepared by the potassium carbonate method, and the cold dark reaction solution when cautiously diluted with water deposited the crystalline iso*indoline*, m. p. 174—175° (E.T., T.I. 163°) (from ethanol) (Found: C, 84·4; H, 6·9; N, 8·3%; *M*, in boiling acetone, 340, 320, 320. $C_{23}H_{22}N_2$ requires C, 84·6; H, 6·8; N, 8·6%; *M*, 326). It sublimed unchanged at 250°/0·04 mm.

The m-*tolyl analogue*, similarly prepared, formed plates, m. p. 145—155°, from ethanol (Found: C, 84·7; H, 7·1. $C_{23}H_{22}N_2$ requires C, 84·6; H, 6·8%).

Reactions of the Iso*indoline* (III; R = Me).—(1) A suspension of the *iso*indoline (0·2 g.) in an excess of 40% aqueous formaldehyde was boiled under reflux for 3 hr., concentrated hydrochloric acid (0·2 c.c.) being added after 30 min. to hasten dissolution. The cold clear solution when poured into aqueous sodium carbonate deposited the unchanged *iso*indoline, m. p. and mixed m. p. 145—149° (E.T.) after crystallisation from ethanol. The compound was recovered after its solution in ethanol–acetone had been saturated with hydrogen chloride and then boiled for 2 hr.

(2) A solution of the *iso*indoline (0·2 g.) in acetic acid–acetic anhydride (1 : 1 v/v; 5 c.c.) was boiled under reflux for 5 hr., becoming bluish-black. The cold solution, when diluted with water and neutralised with 10% aqueous sodium hydroxide, deposited a black solid, which was collected. The filtrate, on ether-extraction, gave acetanilide. The black solid was apparently unaffected by hot aqueous chromic acid.

(3) A solution of sodium dichromate (2 g.) in water (5 c.c.) was added cautiously to one of the *iso*indoline (0·7 g.) in concentrated sulphuric acid (2 c.c.), with heat evolution. The mixture was heated under reflux for 30 min., cooled, and diluted with water (2—3 c.c.). The *N*-phenylphthalimide which was precipitated formed silky needles, m. p. 204—206°, from ethanol (Found: C, 75·3; H, 4·1; N, 6·0. Calc. for $C_{14}H_9O_2N$: C, 75·3; H, 4·1; N, 6·3%). The presence of the phthalimide ring was confirmed by the infrared spectrum.

(4) Bromine water was added dropwise to a solution of the *iso*indoline in dilute hydrobromic acid until a permanent yellow colour developed. Aqueous sodium carbonate precipitated

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a *monobromo-derivative*, m. p. 138—140° (E.T.) after several recrystallisations from aqueous ethanol (Found: C, 67·0; H, 4·6; N, 7·6. $C_{21}H_{17}N_2Br$ requires C, 66·9; H, 4·5; N, 7·4%). The position of the bromine atom has not been determined.

The p-*tolyliso*indoline (as III; R = Me) was recovered unchanged after treatment with (*a*) boiling 20% hydrochloric acid for 6 hr., (*b*) sulphuric acid–water (equal vols.) at 100—110° for 1 hr., (*c*) boiling 20% ethanolic potassium hydroxide (w/v) for 4 hr., (*d*) 2 : 4-dinitrobenzaldehyde (1 mol.) in boiling ethanol for 5 hr., (*e*) potassium permanganate in boiling acetone solution for 10 min. A hot ethanolic solution when treated with sodium (6 equivalents), and an acetic acid solution containing platinum oxide when treated with hydrogen at 20°/55 atm. for 17 hr., furnished the unchanged *iso*indoline.

2-*Phenyl*-1-*phenylimino*iso*indoline* (III; R = H).—Preparation of this compound from *o*-chloromethylbenzonitrile has been described.[1] Its preparation from the corresponding 1-oxo*iso*indoline [1] is now described. A mixture of the 1-oxo-derivative (IV; R = H) (10 g.), aniline (20 c.c., 4 mols.), and phosphorus oxychloride (100 c.c.) was boiled under reflux for 3 hr., cooled, and poured into cold water (3 l.). The solution was filtered to remove a large amount of a green solid, which was triturated with water and again filtered. The united extracts were neutralised with 10% aqueous sodium hydroxide, and the precipitated *iso*indoline (III; R = H), when collected and recrystallised from ethanol, had m. p. 151—153° (E.T.) (Found: C, 84·8; H, 6·0; N, 10·1. Calc. for $C_{20}H_{16}N_2$: C, 84·5; H, 5·7; N, 9·9%). The use of phosphorus trichloride in place of the oxychloride left the 1-oxo-derivative unchanged. An ethereal solution of the *iso*indoline (III; R = H) when treated with hydrogen chloride deposited the hydrochloride, m. p. 240° (E.T., darkening from 233°) after drying at 50° (Found: C, 74·7; H, 5·2. Calc. for $C_{20}H_{16}N_2$,HCl: C, 74·9; H, 5·3%).

3-*Methyl*-2-*phenyl*-1-*phenylimino*iso*indoline* (III; R = Me).—Phthalic anhydride was converted into *o*-carboxybenzoylacetic acid,[9] which was selectively decarboxylated to 2-carboxyacetophenone by Rule and Smith's method.[10] Reduction with sodium amalgam then gave 3-methylphthalide.[11]

The crude phthalide (29 g.), aniline (55 g.), and phosphorus oxychloride (100 c.c.) were heated on a steam-bath for 3 hr. The hot mixture was filtered to remove a copious black solid, and the purple filtrate shaken with charcoal to remove much of the colour. The filtered solution when treated with an excess of dilute aqueous sodium hydroxide deposited a flocculent fine brown solid, which was collected with difficulty, dissolved in ethanol, and reprecipitated with water. Recrystallisation from ethanol afforded in small yield the *iso*indoline (III; R = Me), m. p. alone and mixed with that prepared from the chloride (I), 147—148° (Found: N, 9·2. Calc. for $C_{21}H_{18}N_2$: N, 9·4%).

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 29th*, 1958.]

[9] Gabriel and Neumann, *Ber.*, 1893, **26**, 952.
[10] Rule and Smith, *J.*, 1926, 556.
[11] Gabriel and Michael, *Ber.*, 1887, **10**, 2205; Giebe, *Ber.*, 1896, **29**, 2533.

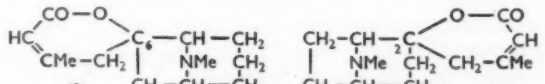
XUM

123. *An Alkaloid of* Dioscorea hispida, *Dennstedt. Part V.* The Degradation of Dioscorinol.*

By J. B. Jones and A. R. Pinder.

Evidence is presented which suggests that the $C_8H_{13}ON$ keto-base obtained by degradation of dioscorinol is tropan-2-one (IV), and not tropan-6-one (III) as proposed by other workers. Dioscorine is therefore formulated as (II), and more exactly as (X).

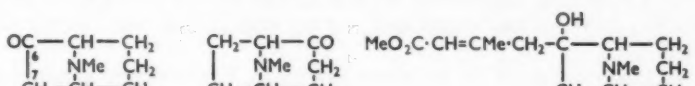
Previous work [1] has shown that in dioscorine, an alkaloid occurring in the tubers of *Dioscorea hispida*, Dennst., an αβ-unsaturated six-membered lactone ring is linked in a *spiro*-manner with a tropane system, in the 2- or 6-position of the latter. Two possible constitutions, (I) and (II), were advanced for the alkaloid, the former being preferred on



(I) (II)

the grounds that it is derived from tropan-6-ol, from which several familiar alkaloids are derived.

Strong evidence favouring structure (I) has been described recently by Büchi, Ayer, and White,[2] who have degraded dioscorine by successive reduction with lithium aluminium hydride, ozonolysis, and alkaline decomposition. The final product was an optically active ketonic base $C_8H_{13}ON$, which on reduction by desulphurisation of its ethylene thioketal, afforded tropane. The compound is therefore a tropanone, and must be formulated as either tropan-6-one (III) or tropan-2-one (IV). For two main reasons, structure (III) was preferred. First, the $C_8H_{13}ON$ base showed a carbonyl infrared band at 1730 cm.$^{-1}$, which these authors considered in better agreement with the location of the carbonyl group in a five-membered ring, as in (III), than with its location in a six-membered ring, as in (IV). Secondly, the tropanone methiodide underwent Hofmann degradation with remarkable facility (sodium hydrogen carbonate at 30°), which gave strong support to structure (III) since here a methylene group β to the nitrogen atom is activated by a neighbouring carbonyl group. No such activation is possible with (IV).



(III) (IV) (V)

Whilst the chemical evidence for the structure of the ketonic base appeared convincing, it seemed to us that the position of the carbonyl band at 1730 cm.$^{-1}$ was, in fact, more in agreement with the presence of the group in a six-membered ring, if the assumption is made that ketonic carbonyl frequencies in heterocyclic nitrogen systems are analogous to those in carbocyclic systems.[3] Nevertheless, we contemplated a synthesis of compound

* Part IV, *Tetrahedron*, 1957, **1**, 301. For a preliminary account of the present results see *Chem. and Ind.*, 1958, 1000.

[1] Pinder, *Chem. and Ind.*, 1957, 1240; *Tetrahedron*, 1957, **1**, 301.

[2] Büchi, Ayer, and White, XVIth Internat. Congress Pure & Applied Chem., Paris, July, 1957.

[3] Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, chapter 9; Jones and Sandorfy, in "Technique of Organic Chemistry," ed. Weissberger, Interscience, New York, 1956, pp. 443 *et seq.*

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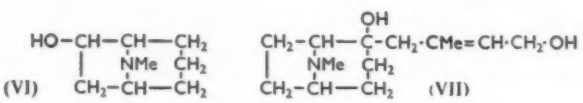
(I) by a Reformatsky condensation between the ketone (III) and methyl γ-bromosenecioate, to give the hydroxy-ester (V), which on hydrolysis and lactonisation would afford the base (I).

A convenient route to tropan-6-one (III) started with 6-hydroxytropinone, available by a Robinson tropinone-type synthesis from maleic dialdehyde, methylamine, and acetonedicarboxylic acid.[4] We have been able to improve this preparation slightly. Wolff–Kishner reduction of the hydroxy-ketone afforded tropan-6-ol (VI), m. p. 65°. A compound formulated as tropan-6β-ol, m. p. 91°, has been described by Kovács and Banfi,[5] who obtained it by successive treatment of tropane-3α : 6β-diol with thionyl chloride and a base, followed by hydrogenation. We have not been able to compare these two products directly, but the infrared spectra of our compound and of 6β-hydroxytropinone in the 3400—3650 cm.$^{-1}$ region are very similar, and we conclude that our product is tropan-6β-ol, the configuration of the 6-hydroxyl group in 6β-hydroxytropinone having been established as β by chemical methods.[6] Kovács and Banfi's product is presumably the 6α-isomer, epimerisation having occurred.



(VI) (VII)

Oxidation of tropan-6β-ol by chromic acid gave, in 25% yield, tropan-6-one (III), together with a considerable amount of unchanged alcohol. Our failure to obtain the ketonic base in good yield, even when more than the theoretical amount of chromic acid was used, is paralleled by the observations that the alkaloid valeroidine [7] (3α-*iso*valeryloxytropan-6β-ol) and 6β-hydroxytropinone [8] are not oxidised to the corresponding ketones by chromic acid or by other methods. Further comment on this behaviour, which is probably explained by interaction between the hydroxyl group and the nitrogen atom, is reserved until the completion of certain model experiments.

Tropan-6-one is a colourless, strongly basic syrup, and in harmony with its structure as an α-amino-ketone is rapidly oxidised in air and reduces ammoniacal silver nitrate and Fehling's solution readily. It shows strong infrared carbonyl bands at 1750 (in CCl_4) and 1752 cm.$^{-1}$ (liquid film), unexpectedly high values compared with that of 1730 cm.$^{-1}$ for the $C_8H_{13}ON$ ketone obtained by Büchi *et al.* (see above). Its methiodide shows a similar band at 1778 cm.$^{-1}$ (Nujol mull).

It appeared from these figures that the degradative ketonic base was not tropan-6-one, so the projected synthesis was abandoned, and the degradation described by Büchi *et al.*[2] was repeated.

Dioscorinol was obtained as described previously [1] by lithium aluminium hydride reduction of dioscorine, purified *via* its picrate. The American workers have apparently obtained this diol as a crystalline compound, m. p. 101°, but in spite of many repetitions we have obtained it only as a thick syrup. Ozonolysis of dioscorinol in acetic acid afforded a saturated, basic keto-alcohol $C_{11}H_{19}O_2N$, showing infrared bands (in CCl_4) at 1718 (saturated, acyclic C=O) and 3535 cm.$^{-1}$ (broad, OH), with strong intramolecular hydrogen-bonding between the two functional groups. It has not so far been possible to prepare a crystalline derivative of this compound: its picrate and methiodide were oils. With

[4] Nedenskov and Clauson-Kaas, *Acta Chem. Scand.*, 1954, **8**, 1295; see also Sheehan and Bloom, *J. Amer. Chem. Soc.*, 1952, **74**, 3825; Stoll, Becker, and Jucker, *Helv. Chim. Acta*, 1952, **35**, 1263; Sandoz, Ltd., B.P. 737,419/1955; Schöpf and Arnold, *Annalen*, 1947, **558**, 109.

[5] Quoted by Fodor, Tóth, Koczor, and Vincze, *Chem. and Ind.*, 1955, 1260.

[6] Fodor and Kovács, *J.*, 1953, 2341; Fodor, Tóth, and Vincze, *Helv. Chim. Acta*, 1954, **37**, 907; Fodor, *Tetrahedron*, 1957, **1**, 94.

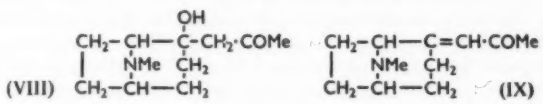
[7] Martin and Mitchell, *J.*, 1940, 1155.

[8] Meinwald and Chapman, *J. Amer. Chem. Soc.*, 1958, **80**, 633.

Brady's reagent it gave a deep red precipitate, suggestive of the presence of an αβ-unsaturated carbonyl grouping, although the base itself showed no intense absorption in the ultraviolet region. We have confirmed the previous observation [1,2] that the base gives a positive iodoform test, and therefore contains a $CH_3 \cdot CO \cdot C\leqslant$ grouping.

We have confirmed also that the ozonolysis product, in warm dilute alkali, breaks down into acetone and a syrupy ketonic base $C_8H_{13}ON$. This base is presumably the same as that isolated by Büchi *et al.*,[2] although it shows infrared carbonyl bands at 1737 (liquid film) and 1740 cm.$^{-1}$ (in CCl_4); its methiodide shows a similar band at 1720 cm.$^{-1}$. An infrared comparison between this base and synthetic tropan-6-one differentiated the two compounds; this was confirmed by a similar comparison of the two crystalline picrates and methiodides, and the two methiodides showed a depression in m. p. on admixture. These differences were too pronounced to be ascribed merely to the fact that the " natural " ketone is optically active, and the synthetic product racemic, and in any case such a difference would not be manifest in the infrared curves, in the liquid state or in solution.[9]

We have not yet obtained a sufficient quantity of the degradative base $C_8H_{13}ON$ to confirm that on reduction by desulphurisation of its ethylene thioketal it yields tropane, although we have not been able to reduce tropinone or 6β-hydroxytropinone by this method, owing to our inability to prepare their ethylene thioketals under the usual conditions. If we accept the validity of this step, and recall earlier evidence [10] for the presence of a tropane system in dioscorine, the only possible structure for the $C_8H_{13}ON$ base is apparently that of tropan-2-one (IV), and dioscorine is to be formulated as (II). Dioscorinol therefore has structure (VII), and the ozonolysis product is the aldol (VIII), which on treatment with alkali undergoes retroaldol cleavage to acetone and the ketone (IV). The reaction of the aldol (VIII) towards Brady's reagent is explained by a preliminary dehydration to the αβ-unsaturated ketone (IX).



(VIII) (IX)

The position of the carbonyl band of tropan-6-one (III) at a somewhat high wavenumber than that for *cyclo*pentanones has prompted us to study the infrared spectra of several model ketones. Little has been recorded concerning the position of carbonyl absorption in heterocyclic ketones such as 3-oxopyrrolidine and 3- and 4-oxopiperidine. Our investigations will be described in detail later, but a few preliminary results indicate that in 1-methyl-3-oxopyrrolidine the carbonyl stretching band occurs at a higher frequency (1765 cm.$^{-1}$) than in *cyclo*pentanone (1745 cm.$^{-1}$). A similar effect is noted with *N*-substituted 2 : 3-dioxopyrrolidines,[11] and a smaller one with 1-methyl-4-oxopiperidine and tropinone, compared with *cyclo*hexanone. We conclude that the carbonyl frequency of 1730 cm.$^{-1}$, quoted by Büchi *et al.*,[2] is too low to accommodate the presence of a 1-methyl-3-oxopyrrolidine system in the $C_8H_{13}ON$ ketone.

The ease of Hofmann decomposition of the $C_8H_{13}ON$ keto-base, mentioned by the American workers, led us to study the effect of the mild conditions specified on tropan-6-one methiodide. We found that this quaternary salt was stable to aqueous sodium hydrogen carbonate at 30° for several hours. Even when the temperature was raised to 60° for 6 hr. the methiodide was mainly recovered unchanged. It is of interest that in tropinone two methylene groups β to the nitrogen atom are activated by the carbonyl group, yet the

[9] Jones and Sandorfy, ref. 3, p. 324.
[10] Pinder, *J.*, 1956, 1577.
[11] Southwick, Previc, Casanova, and Carlson, *J. Org. Chem.*, 1956, **21**, 1087; Vaughan and Covey, *J. Amer. Chem. Soc.*, 1958, **80**, 2197.

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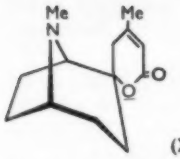
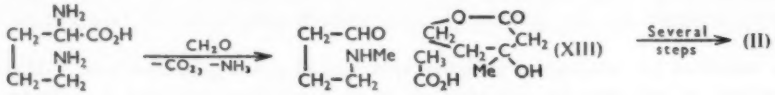
methiodides of this base [12] and of several substituted tropinones [8,13] and compounds of analogous structure [14] require treatment with base at 100° for decomposition. We have found that tropinone methiodide is stable to aqueous sodium hydrogen carbonate at 30° for 24 hr., and previous workers [12] have shown that steam distillation with this reagent for 30 min. is necessary for decomposition.



(X)

As a result of our earlier infrared studies [1] on dihydrodeoxydioscorinol we may write the three-dimensional structure (X) as a more accurate representation of dioscorine.

From the biogenetic viewpoint the structure (II) may perhaps be derived from ornithine (XI) [*via* γ-methylaminobutyraldehyde (XII)], mevalonic lactone (XIII), and acetic acid (1 mol.), according to the annexed scheme.[17]



(XI) (XII)

Experimental

6β-*Hydroxytropinone*.—This compound was most conveniently prepared from 2 : 5-dihydro-2 : 5-dimethoxyfuran [15] (hydrolysed and hydrated *in situ* to maleic dialdehyde), methylamine hydrochloride, and acetonedicarboxylic acid, essentially as outlined by Nedenskov and Clauson-Kaas.[4] Continuous ether-extraction for several days gave a nicely crystalline product which, recrystallised from benzene, had m. p. 123° (yield 35—40%), $\nu_{max.}$ (in CCl_4) 1718 (C=O), 3450 (broad), 3598, and 3635 cm.$^{-1}$ (all OH).

Tropan-6β-*ol* (VI).—6β-Hydroxytropinone (4·16 g.) in ethanol (40 c.c.) was heated with 100% hydrazine hydrate (8·4 g.) at 100° for 2 hr., the ethanol being allowed to distil off gradually. The solvents were then removed under reduced pressure and the syrupy hydrazone was heated with powdered potassium hydroxide (8·0 g.) at 100° for 2 hr., then at 150° for a further hr. The total nitrogen evolution corresponded to 1 mol. The solid residue was cooled and thoroughly extracted with boiling ether, and the extract dried (K_2CO_3) and evaporated, leaving *tropan*-6β-*ol* (3·0 g.), b. p. 87—90°/0·1 mm. (2·75 g.). The distillate solidified, and crystallised from light petroleum (b. p. 40—60°) in rhombic prisms, m. p. 65° (Found: C, 67·7; H, 10·4; N, 9·5. $C_8H_{15}ON$ requires C, 68·1; H, 10·6; N, 9·9%), hydroxyl bands (in CCl_4) at 3450 (broad), 3601, and 3635 cm.$^{-1}$. The *picrate* separated from methanol in yellow needles, m. p. 259° (decomp.) (Found: C, 45·1; H, 4·7; N, 15·3. $C_{14}H_{18}O_8N_4$ requires C, 45·4; H, 4·9; N, 15·2%). The *methobromide* crystallised from ethanol in rhombs, m. p. >330° (Found: C, 45·6; H, 7·3; N, 5·6. $C_9H_{10}ONBr$ requires C, 45·75; H, 7·6; N, 5·9%). Treatment of the base with ethanolic hydrogen peroxide afforded the syrupy amine oxide, the *picrate* of which separated from ethanol in yellow needles, m. p. 225° (decomp.) (Found: C, 43·5; H, 4·5; N, 14·2. $C_{14}H_{18}O_9N_4$ requires C, 43·5; H, 4·65; N, 14·5%).

Tropan-6-*one* (III).—To a solution of tropan-6β-ol (4·7 g.) in acetic acid (40 c.c.), previously heated to 60—70°, was added gradually, during 15 min., with stirring, chromic acid (2·34 g.) dissolved in water (2 c.c.) and acetic acid (10 c.c.). The mixture was heated at 85—90° for 3 hr., then cooled, diluted with water (100 c.c.), basified with excess of solid potassium carbonate, and subjected to continuous ether-extraction for 24 hr. Evaporation of the dried (Na_2SO_4) extract gave a brown oil (3·0 g.), which when fractionated *via* a short Vigreux column yielded *tropan*-6-*one*, b. p. 78—90°/6 mm. (1·05 g.), unchanged tropan-6β-ol, b. p. 109—111°/6 mm., m. p. 65°

[12] Büchi, Yang, Emerman, and Meinwald, *Chem. and Ind.*, 1953, 1063; *J. Amer. Chem. Soc*. 1955, **77**, 4401.
[13] Meinwald and Chapman, *ibid.*, 1956, **78**, 4816; van Tamelen, Barth, and Lornitzo, *ibid.*, 1956, **78**, 5442.
[14] Meinwald and Koskenkyla, *Chem. and Ind.*, 1955, 476.
[15] Imperial Chemical Industries (Billingham Division), Ltd., personal communication; T. and H. Smith, Ltd., B.P. 703,929/1954.

(1·25 g.), and involatile residue (0·7 g.). The keto-base, purified *via* its crystalline picrate (see below) with decomposition with ammonia, distilled at 82°/7 mm. (Found: C, 69·5; H, 9·35; N, 10·3. $C_8H_{13}ON$ requires C, 69·1; H, 9·35; N, 10·0%), C=O bands (in CCl_4) at 1750 and 1752 cm.$^{-1}$ (liquid film). Tropan-6-one is a colourless syrup rapidly oxidised by air; it reduces ammoniacal silver nitrate and Fehling's solution readily. The *picrate* separated from 50% aqueous ethanol in yellow needles, m. p. 269° (decomp.) (Found: C, 46·0; H, 4·2; N, 15·2. $C_{14}H_{16}O_8N_4$ requires C, 45·7; H, 4·4; N, 15·2%), C=O band (in KCl) at 1770 cm.$^{-1}$. The *methiodide* crystallised from aqueous ethanol in rhombic prisms, m. p. 289° (decomp.) or 303—304° (decomp.) (Found: C, 38·7; H, 6·2; N, 5·0. $C_9H_{16}ONI$ requires C, 38·4; H, 5·7; N, 5·0%). C=O band (in Nujol mull) at 1778 cm.$^{-1}$.

Dioscorine.—The alkaloid, obtained as described previously,[16] was purified *via* its picrate,[16] which was prepared in methanol solution in the usual manner, recrystallised from acetone, collected, dried in air, suspended in ether, and shaken repeatedly with ice-cold, 50% potassium hydroxide solution until the aqueous layer was no longer coloured. The dried, ethereal solution was evaporated, and the residual alkaloid distilled (b. p. 140—145°/0·2 mm.). It crystallised readily overnight and had $[\alpha]_D^{20}$ −32·0° (in chloroform, *c* 3·4), $\lambda_{max.}$ (in methanol) 215 mμ (ε 10,160).*

Ozonolysis of Dioscorinol.[1]—Dioscorinol [1] (3·6 g.) in glacial acetic acid (30 c.c.) was ozonised for 5 hr. at 15°. To the cooled solution zinc dust (1·5 g.) was added, and the mixture kept for 2 hr., with occasional shaking, by which time the starch–iodide test was negative. After filtration, water (50 c.c.) was added to the solution, which was then rendered strongly alkaline with potassium carbonate at <20°. Continuous ether-extraction for 48 hr. yielded, after drying (K_2CO_3) and evaporation, a brown, viscous oil (3·0 g.), which distilled at 80°/0·01 mm., 90—92°/0·04 mm. (1·0 g.) (Found: C, 67·5; H, 9·8; N, 7·3. $C_{11}H_{19}O_2N$ requires C, 67·0; H, 9·4; N, 7·1%), $\nu_{max.}$ (in CCl_4) 1718 (C=O) and 3535 cm.$^{-1}$ (broad, OH), having no intense absorption in the ultraviolet region. This product, considered to be 2-*acetonyltropan*-2-*ol* (VIII), formed an oily picrate and methiodide. With 2 : 4-dinitrophenylhydrazine in ethanolic sulphuric acid it gave a deep red precipitate, indicative of dehydration. It gave a positive iodoform reaction.

Alkaline Decomposition of the Ozonolysis Product.—(*a*) The above ozonolysis product (1·0 g.) was heated on the water-bath for 30 min. with 0·2N-sodium hydroxide (50 c.c.). The cooled solution was saturated with potassium carbonate and extracted continuously with ether for 24 hr. Distillation of the dried (Na_2SO_4) extract gave an *oil* (0·7 g.), b. p. 89—90°/8 mm. (0·25 g.), which was converted into its picrate in methanol. The *picrate* crystallisedf rom 50% aqueous ethanol in yellow needles, m. p. 188° (decomp.) (Found: C, 46·2; H, 4·6; N, 14·9. $C_{14}H_{16}O_8N_4$ requires C, 45·7; H, 4·4; N, 15·2%), C=O band (in KCl) at 1750 cm.$^{-1}$. Alkaline decomposition of the picrate afforded a colourless oily base, b. p. 102°/14 mm. (Found: C, 68·6; H, 9·3; N, 9·7. $C_8H_{13}ON$ requires C, 69·1; H, 9·35; N, 10·0), C=O bands at 1737 (liquid film) and 1740 cm.$^{-1}$ (in CCl_4). This product, considered to be tropan-2-one (IV), showed reactions characteristic of a ketonic tertiary base; the *methiodide* separated from aqueous ethanol in rhombic prisms, m. p. 295° (decomp.) (Found: C, 38·1; H, 5·8. $C_9H_{16}ONI$ requires C, 38·4; H, 5·7%), C=O band (in Nujol mull) at 1720 cm.$^{-1}$. A mixture of this methiodide and tropan-6-one methiodide, m. p. 289° (decomp.) (see above), had m. p. 282—283° (decomp.), with previous softening.

(*b*) A mixture of the ozonolysis product (1·0 g.) and 0·2N-sodium hydroxide (50 c.c.) was distilled until about 25 c.c. of distillate had been collected. Addition of an excess of a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N-sulphuric acid gave a yellow precipitate which crystallised from ethanol in yellow needles, m. p. 126—127°, alone or mixed with acetone 2 : 4-dinitrophenylhydrazone.

We thank Sir Robert Robinson, O.M., F.R.S., and Dr. W. Klyne for their interest in this work, and we are indebted to Dr. G. Eglinton for the infrared measurements (carried out by Mr. F. Gisbey). Plant material was supplied by the Colonial Products Council and extraction

* A misprint occurs in Part I of this series:[16] *on* p. 2238 *for* ε 16,160 *read* ε 10,160.

[16] Pinder, *J.*, 1952, 2236.

[17] Cf. James, in "The Alkaloids," ed. Manske and Holmes, Academic Press Inc., New York, 1950, Vol. I, pp. 56 *et seq.*; Robinson, "The Structural Relations of Natural Products," Clarendon Press, Oxford, 1955, pp. 59 *et seq.*

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facilities were placed at our disposal by Dr. F. R. Smith (Messrs. T. and H. Smith, Ltd.), whom we also thank. One of us (J. B. J.) is grateful to the Department of Scientific and Industrial Research for a maintenance grant.

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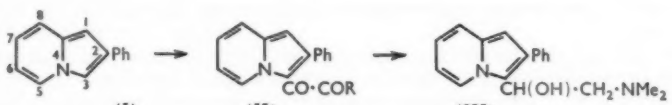
124. *The Preparation of Aminoalkylpyrrocolines.*

By D. E. AMES, T. F. GREY, and W. A. JONES.

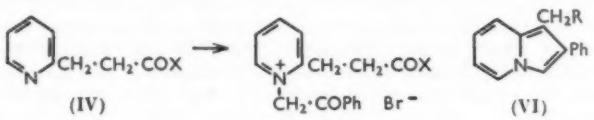
Oxalyl chloride condenses readily with 2-phenylpyrrocoline to give 2-phenylpyrrocoline-3-glyoxylyl chloride which on treatment with dimethylamine followed by lithium aluminium hydride affords 3-(2-dimethylamino-1-hydroxyethyl)-2-phenylpyrrocoline. An aminoethylpyrrocoline was, however, obtained by an alternative route.

THE pharmacological properties of serotonin and other tryptamine derivatives suggested that the synthesis of analogous aminoethylpyrrocoline derivatives would be of interest. The readily-available 2-phenylpyrrocoline was used as starting material. In view of the rapidity with which oxalyl chloride condenses with indoles in the absence of catalyst,[1] the condensation of oxalyl chloride with 2-phenylpyrrocoline in ether was examined. The resulting crystalline acid chloride (II; R = Cl) was readily converted into amides (II; R = NH_2 and NMe_2). The acyl group is presumed to have entered the 3-position by analogy with the uncatalysed benzoylation of pyrrocoline [2] and 2-phenylpyrrocoline [3] in the 3-position.



(I) (II) (III)

Reduction of the amide (II; R = NMe_2) with lithium aluminium hydride gave the hydroxyamine (III) in small yield. It is of interest that the hydroxyl group was not lost by hydrogenolysis, as occurs in the corresponding reduction of 3-indolylglyoxyl amides other than the 1-alkyl compounds.[4]



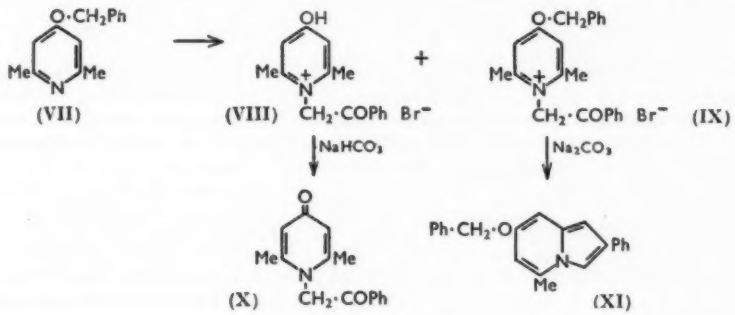
(IV) (V) (VI)

An alternative approach was therefore required for the synthesis of a pyrrocoline bearing an aminoethyl group. Condensation of the ester (IV; X = OEt) with phenacyl bromide gave the quaternary salt (V; X = OEt) but this could not be cyclised to a pyrrocoline. The corresponding amide (IV; X = NH_2) did, however, yield the pyrrocoline (VI; R = $CO{\cdot}NH_2$), which was reduced with lithium aluminium hydride to 1-aminoethyl-2-phenylpyrrocoline (VI; R = $CH_2{\cdot}NH_2$), isolated as the dipicrate.

Although it appears that no hydroxypyrrocolines have been described, some preliminary experiments were made to examine the possibility of preparing an aminoalkyl-hydroxy-

[1] Speeter and Anthony, *J. Amer. Chem. Soc.*, 1954, **76**, 6208 and references cited therein.
[2] Scholtz and Fraude, *Ber.*, 1913, **46**, 1069.
[3] Borrows, Holland, and Kenyon, *J.*, 1946, 1069; Borrows and Holland, *Chem. Rev.*, 1948, **42**, 611.
[4] Clemo, Morgan, and Raper, *J.*, 1935, 1744.

pyrrocoline. 4-Chloro-2 : 6-dimethylpyridine was converted into the 4-benzyloxy-compound (VII) by the action of potassium benzyl oxide. Quaternisation with phenacyl bromide then yielded a mixture from which the salt (VIII), formed by debenzylation, was isolated. Treatment of this with sodium hydrogen carbonate solution yielded 2 : 6-dimethyl-1-phenacylpyrid-4-one (X) and not a pyrrocoline. However, when the non-crystalline part of the quaternisation products, presumably containing the benzyloxy-compound (IX), was



treated with sodium carbonate solution, crystalline 7-benzyloxy-5-methyl-2-phenylpyrrocoline (XI) was obtained in very small yield. An attempt to remove the benzyl group by catalytic hydrogenation in the presence of palladised strontium carbonate was unsuccessful. The low yield of benzyloxy-compound (XI) prevented its use in further synthesis.

Experimental

2-Phenyl-3-pyrrocolinylglyoxylyl Chloride.—Oxalyl chloride (25 g.) was added gradually to a suspension of 2-phenylpyrrocoline [3] (30 g.) in ether (50 c.c.) and benzene (300 c.c.), and the mixture was left at room temperature for 4 hr. The crude *product* was filtered off and recrystallised from benzene–light petroleum (b. p. 60—80°) to give green material [75%; m. p. 110—114° (decomp.)]. Further recrystallisation furnished yellow prisms, m. p. 114—115° (decomp.) (Found: C, H, 3·4; Cl, 12·3. $C_{16}H_{10}O_2NCl$ requires C, 67·6; H, 3·4; Cl, 11·9%).

NN-Dimethyl-2-phenyl-3-pyrrocolinylglyoxylamide.—A stirred solution of the acid chloride (15 g.) in benzene (250 c.c.) was cooled while excess of dimethylamine was passed in. The mixture was left at room temperature for 2 hr., then filtered; the solid was taken up in chloroform (100 c.c.) and washed with 2N-sodium hydroxide and water, dried (Na_2SO_4), and evaporated. Recrystallisation from 2-methoxyethanol furnished the *amide* (11 g.), yellow needles, m. p. 198—200° (Found: C, 73·9; H, 5·4; N, 9·6. $C_{18}H_{16}O_2N_2$ requires C, 74·0; H, 5·5; N, 9·6%), $\lambda_{max.}$ 2350 (ε 22,600), 2650 (ε 16,900) and 3810 Å (ε 17,400) in ethanol.

2-Phenyl-3-pyrrocolinylglyoxylamide, prepared similarly, formed yellow needles, m. p. 178—181°, from ethyl acetate (Found: C, 72·8; H, 4·5; N, 11·0. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·6; N, 10·6%).

3-(2-Dimethylamino-1-hydroxyethyl)-2-phenylpyrrocoline.—A solution of the foregoing dimethylamide (4·6 g.) in tetrahydrofuran (100 c.c., dried over CaH_2) was added gradually to lithium aluminium hydride (2 g.) in tetrahydrofuran (100 c.c.) at room temperature. The mixture was refluxed for 1 hr. and left overnight. After addition of ethyl acetate (25 c.c.) and then water (5 c.c.), the mixture was refluxed for 15 min. and filtered, the solid being washed with ethyl acetate. Evaporation *in vacuo* (bath 30°) gave a gum which crystallised on trituration with methanol. Fractional crystallisation from methanol yielded 0·25 g. of material, m. p. 99—103°, from which the *hydroxy-amine* was obtained as prisms, m. p. 112—115°, by further crystallisation (Found: C, 77·1; H, 7·2; N, 9·9. $C_{18}H_{20}ON_2$ requires C, 77·1; H, 7·2; N, 10·0%).

2-2′-Ethoxycarbonylethyl-1-phenacylpyridinium Bromide.—A solution of ethyl 3-2′-pyridylpropionate [4] (10 g.) and phenacyl bromide (11·1 g.) in acetone (25 c.c.) was set aside for 1 hr., then refluxed for 3·5 hr. The *salt*, which separated on cooling, formed needles, m. p. 154—155°,

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from butan-2-one–ethanol (Found: C, 57·4; H, 5·2; Br, 21·1. $C_{18}H_{20}O_3NBr$ requires C, 57·2; H, 5·3; Br, 21·1%). Attempts to cyclise the compound by treatment with sodium hydrogen carbonate solution were unsuccessful.

2-Phenyl-1-pyrrocolinylacetamide.—β-2-Pyridylpropionamide [5] (8·2 g.) and phenacyl bromide (11 g.) in butan-2-one (150 c.c.) were refluxed for 8·5 hr. The supernatant liquid was decanted from gummy residue which was then boiled with water (100 c.c.). The hot aqueous solution was filtered (charcoal) and sodium hydrogen carbonate (40 g.) added. On cooling, crude product separated (3·8 g.; m. p. 165—169°). Recrystallisation from butan-2-one furnished the *pyrrocoline* as needles, m. p. 168—170° (Found: C, 76·6; H, 5·6; N, 11·3. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%).

1-2′-Aminoethyl-2-phenylpyrrocoline.—The amide (2·8 g.) was reduced with lithium aluminium hydride (1·0 g.) in ether (100 c.c.) (Soxhlet extraction for 6 hr.). After addition of ethyl acetate (10 c.c.) and 5N-sodium hydroxide (3 c.c.) the mixture was filtered and the filtrate evaporated *in vacuo*. The residue was treated with methanolic picric acid, to give the *dipicrate*, m. p. 135—136°, of the amine as prisms from aqueous ethanol (Found: C, 47·9; H, 3·9; N, 15·7. $C_{28}H_{22}O_{14}N_8$ requires C, 48·4; H, 3·2; N, 16·1%). Starting material (2·1 g.) was recovered from the Soxhlet thimble. No product was isolated on reduction in tetrahydrofuran.

4-Benzyloxy-2 : 6-dimethylpyridine.—A solution of potassium hydroxide (48 g.) in benzyl alcohol (630 c.c.) and xylene (130 c.c.) was refluxed through a phase-separator (Dean and Stark) until all the water had been removed. 4-Chloro-2 : 6-dimethylpyridine [6] (48 g.) was then added and the mixture was heated at 210° (bath) for 2 hr. The cooled solution was poured into water, and the product isolated with ethyl acetate. Fractional distillation through a short Fenske column yielded the *benzyloxypyridine*, b. p. 130°/0·8 mm., n_D^{20} 1·5653 (Found: C, 78·8; H, 6·9. $C_{14}H_{15}ON$ requires C, 78·8; H, 7·1%).

Quaternisation of 4-Benzyloxy-2 : 6-dimethylpyridine with Phenacyl Bromide.—The benzyloxypyridine (15 g.) and phenacyl bromide (14·5 g.) in butanol (75 c.c.) were left at room temperature overnight and then heated on a steam-bath for 5 hr. The gum obtained by evaporation *in vacuo* partially crystallised on trituration with acetone. *4-Hydroxy-2 : 6-dimethyl-1-phenacylpyridinium bromide* [2·7 g.; m. p. 207—210° (decomp.)] was collected and recrystallised from ethanol; it formed plates, m. p. 214—215° (Found: C, 55·8; H, 5·0; N, 4·2; Br, 24·2. $C_{15}H_{14}O_2NBr$ requires C, 55·9; H, 5·0; N, 4·3; Br, 24·8%). Evaporation of the acetone filtrate gave a gum from which the benzyloxy-compound could not be isolated.

2 : 6-Dimethyl-1-phenacylpyrid-4-one.—The foregoing quaternary salt was warmed with sodium hydrogen carbonate solution and the cooled mixture was filtered. Recrystallisation from benzene–light petroleum (b. p. 60—80°) afforded plates of the *pyridone*, m. p. 103—104° (Found: C, 74·3; H, 6·2. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3%), $\lambda_{max.}$ 2450 Å (ε 14,200) in ethanol.

7-Benzyloxy-5-methyl-2-phenylpyrrocoline.—The residual gum from the above quaternisation was boiled with water (300 c.c.) while sodium carbonate (35 g.) was added in portions. The cooled liquid was extracted with ether, and the extracts were washed with water, dried (K_2CO_3), and evaporated. On trituration with benzene–light petroleum (b. p. 40—60°), some solid (0·4 g.), m. p. 145—151°, was obtained. The *pyrrocoline* recrystallised from the same solvents as needles, m. p. 152—153° (Found: C, 84·2; H, 6·1; N, 5·0. $C_{22}H_{19}ON$ requires C, 84·3; H, 6·1; N, 4·5%), $\lambda_{max.}$ 2600 Å (ε 27,100) in ethanol.

The authors are grateful to Dr. R. E. Bowman for helpful discussions, to Mr. F. H. Oliver for microanalyses, and to Miss E. M. Tanner for spectroscopic measurements.

RESEARCH DEPARTMENT, PARKE, DAVIS & CO. LTD.,
HOUNSLOW, MIDDLESEX. [*Received, October 8th*, 1958.]

[5] Walter, Hunt, and Fosbinder, *J. Amer. Chem. Soc.*, 1941, **63**, 2771.
[6] Kato and Ohta, *J. Pharm. Soc. Japan*, 1952, **71**, 217; *Chem. Abs.*, 1952, **46**, 4541.

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125. *Covalency and the Iron Group of Complexes.*

By T. M. Dunn.

The covalent character of the bonds in first-row transition-metal hydrates and other complexes is considered from a number of points of view. Pauling's electroneutrality principle appears to apply in the sense that in both di- and tri-positive metal-ion complexes the metal ion attains a local electrical condition close to neutrality at the expense of its ligands. This conclusion is reached by a consideration of ionisation potentials, ligand-field perturbations, and spin–orbit coupling-constant data.

Until relatively recently many inorganic complexes were thought of as either predominantly "ionic" or predominantly "covalent" with respect to their magnetic moments and in their reactions. Which view was taken depended upon the property under consideration and, to a large extent, upon the interpretative theory used. The successes of ligand-field theory (crystal field approximation) emphasised the ionic point of view, although several writers (*e.g.*, Owen [1] and Stevens [2]) have recognised that this cannot be rigidly maintained and a molecular-orbital point of view allowing partial covalent character has sometimes been adopted.

It is interesting to consider the degree to which, in the light of such discussions, the overall charge on the central metal can be treated according to the electroneutrality principle. As early as 1948, Pauling [3] enunciated the postulate "of the essential electrical neutrality of the atoms in a complex" in which he assumed that the net charge is very evenly distributed so that there is always less than about one positive or negative charge on any one atom. This is equivalent to rejecting highly charged structures as unimportant in the final resonance hybrid, even though magnetically and, to some extent, spectroscopically the central atom sometimes behaves almost as a field-free ion.

Such a postulate requires charge transfer to or from the central ion (depending upon whether the formal charge on the central ion is positive or negative) through the formation of a co-ordinate bond. That this charge transfer does in fact occur, as well as its magnitude, can be inferred from several independent types of data.

(1) *Reductions in the Free Atom Term Separations.*—In 1951, Abragam and Pryce [4] in a study of the paramagnetic resonance of crystalline $Co(NH_4)_2(SO_4)_2,6H_2O$, *i.e.*, Co(II), observed that to obtain agreement with experiment it was necessary to postulate that the lowest excited quartet term [5] (^4P) lay only about 11,500 cm.$^{-1}$ higher than the ground term (^4F) instead of 14,560 cm.$^{-1}$ higher as in the free ion.

This reduction in free ion term separation for a complex has been observed by Tanabe and Sugano,[6] Owen,[1] Orgel,[7] and Stevens,[2] all of whom found that the free ion values were not consistent with the interpretation of the spectra of complexes containing the ion. The matter has since been taken up by Jørgensen in some detail, particularly for manganese [8] and nickel [9] complexes.

He considered that the reductions in the term separations (which are equivalent to a reduction in the magnitude of the interelectronic repulsion integrals variously described by their Slater–Condon parameters [10] F_k or by their Racah parameters [11] A, B, C) could

[1] Owen, *Proc. Roy. Soc.*, 1955, *A*, **227**, 183; *Discuss. Faraday Soc.*, 1955, **19**, 127.
[2] Stevens, *Proc. Roy. Soc.*, 1953, *A*, **219**, 542.
[3] Pauling, *J.*, 1948, 1461.
[4] Abragam and Pryce, *Proc. Roy. Soc.*, 1951, *A*, **206**, 173.
[5] "Atomic Energy Levels," Vol. II, Nat. Bureau of Standards (U.S.A.) (1952).
[6] Tanabe and Sugano, *J. Phys. Soc.* (*Japan*), 1954, **9**, 766.
[7] Orgel, *J. Chem. Phys.*, 1955, **23**, 1824.
[8] Jørgensen, *Acta Chem. Scand.*, 1957, **11**, 53.
[9] Bostrup and Jørgensen, *ibid.*, p. 1223.
[10] Condon and Shortley, "Theory of Atomic Spectra," Cambridge Univ. Press, 1953.
[11] Racah, *Phys. Rev.*, 1943, **63**, 367.

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arise from (*a*) the shielding of the central field by electrons donated from the ligands and/or (*b*) spreading of the partially filled *d* shell over the ligands, thereby increasing the available orbital space.

Jørgensen found (*b*) proved [8] but did not comment further upon (*a*).

Possibility (*b*) will, however, result from (*a*) if it is not merely due to a pure crystal field effect, *i.e.*, if the delocalisation is not caused simply by a reduction in the effective central field potential in which the *d* electrons move, owing to the ligands' screening off the outer parts of the orbits without actual charge transfer. In the event of charge transfer, however, it is by no means clear that (*a*) and (*b*) are, or even should be, essentially independent. Rather, (*b*) merely reflects the extent to which (*a*) has occurred since it has been amply shown [12] that the overlap between a 3*d* orbital on, say, a triply positive central ion and an orbital on a ligand such as water is negligible in the absence of some equalising perturbation, the 3*d* orbital being too tight or the ligand orbital too diffuse to overlap efficiently.

With this in mind, consider the term separations E of free atoms or ions and the changes which occur upon electron-transfer. In Table 1 the term separations known from atomic spectra [3] are compared with the experimental values,[1] E', found for the same ions in hexahydrate complexes from transitions which correlate with the atomic $^{\tau}F$–$^{\tau}P$ transitions for zero perturbing fields. The latter values are compared with the separations found for isoelectronic ionic species differing only in their net charges.

TABLE 1. *Term separations (energies in cm.$^{-1}$).*

Metal	Interval	E	E' complex	B(i)	B'(iii)	B(ii)
V(III)	^3F–^3P	12,925	9,300	863	620	863
Ti(II)		10,420		695		755
Sc(I)		7,220		481		500
Cr(III)	^4F–^4P	13,770	10,200	918	680	918
V(II)		11,333	9,000	755	600	810
Ti(I) *		8,366		558		720
Co(II)	^4F–^4P	14,560	12,500	970	833	970
Fe(I)		11,196		746		843
Ni(II)	^3F–^3P	15,836	14,000	1030	933	1030
Co(I)		12,649		843		1000

* This value may be low, owing to the presence of a d^8s ^4F ground term only 860 cm.$^{-1}$ below the d^8 F term.

Table 1 shows that the values of the term separations in the complexes all lie between those for the singly and the doubly charged isoelectronic ionic species independently of whether the formal charge on the complex is three or two. The Racah B values are also included in Table 1 ($B = F_2 - 5F_4$ and the $^{\tau}F - {}^{\tau}P$ separation in free atoms is $15B$) and they are of three types: (i) The B values of isoelectronic ionic species of lower net charge; (ii) those calculated for less highly charged ions of the same atomic number but differing only in the number of *d* electrons present, *e.g.*, V(III), V(II), V(I); (iii) The experimental values.

It might be expected that the values of type (ii) would be better for comparison than those of type (i): nevertheless there should not be radical differences between them (as is clear from the values given), because the B values of a series of mono-, di-, or tri-positive ions increase with atomic number. For nickel(I) the configuration d^8s must be used to obtain a B value of type (ii).

Comparison of the experimental values of B with those of types (i) and (ii) suggests strongly in both cases that the central ion has approximately a single net positive charge, though for nickel(II) the result is uncertain, possibly owing to the large value of the spin–orbit coupling effects discussed by Bostrup and Jørgensen [9] (but even here on a straights interpretation the central atom would be closer to uncharged).

[12] Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, **332**, 354.

By themselves these B values and term separations could be explained on either of the original bases with no distinction between the two subclassifications of (ii), but the closely coincident sets of B values suggest a simple interpretation of 1—2 electrons transferred to the central ion for dipositive and tripositive ions respectively. Further evidence is also available from results discussed in the next section.

(2) *Reduced Spin–Orbit Coupling Constants in Complexes.*—Owen [1] first drew attention to the fact that in many cases the spin–orbit coupling constants of ions involved in complexes, λ'' (these being found from paramagnetic resonance studies on the solid), are much lower than those for the free ion, λ, and he defined $\alpha^2 = \lambda''/\lambda$ as being a measure of the covalence tendencies. For $Ni(H_2O)_6^{2+}$ $\alpha^2 = 0{\cdot}83$ and Owen describes this as the d_γ^* electrons spending 83% of the time in the central ion d_γ orbitals and about 3% in the σ^* orbitals essentially localised on the oxygen atoms.

Following the previous discussion, it seems meaningful to consider the reduction in λ as being due to simple charge-transfer from the ligands to the central metal ion. That this is so, as well as the magnitude of the transfer, is suggested by a comparison of the one-electron spin–orbit coupling parameters ζ_{3d}, obtained from atomic spectra,[5] with those given by Owen [1] (his λ and λ'' values need to be multiplied by the factor $2S$, S being the total spin, to convert them to ζ and ζ'' values respectively).

TABLE 2. (*Energies in cm.*$^{-1}$.)

Metal	Term	λ (free ion)	ζ_{3d}	ζ_{3d}M(II)	ζ_{3d}M(I)	ζ''_{3d}
V(III)	^3F	104	208	165	135	128
Cr(III)	^4F	91	273	225	185	171
V(II)	^4F	55·5	166·5		135	132
Ni(II)	^3F	−324	648		600	540

Table 2 compares the experimental values obtained [1] for the complexes ζ''_{3d} with the values known [5] from the d^n configurations of the same ion with lower net charge. This Table again shows close agreement between columns 6 and 7 and in fact $\zeta''_{3d} < \zeta_{3d}$ M(I). Nickel is again an exception, but the experimental value is at least lower than the ζ_{3d} M(I) value. It is possible to obtain an estimate of ζ_{3d} M(0) for nickel since, even though the configuration d^{10} obviously cannot yield a value, for all the transition-metal ions the spin–orbit constants for the neutral atom with configuration d^ns^2 is almost identical with that of the unipositive ion with configuration d^ns and this is, in turn, almost identical with the dipositive ion with configuration d^n. This allows a value of ζ_{3d} for Ni(IV) in the configuration d^7 to be placed equal to the value known for Ni(III) having the configuration d^7s, and the smooth curve so obtained for configurations d^7, d^8, and d^9 is then extrapolated to d^{10}. The value so obtained is in the range 500—550 cm.$^{-1}$ and probably near the latter figure so that again the nickel atom might somewhat naïvely be assumed to be effectively uncharged.

Since for a hydrogen-like atom or ion with nuclear charge Z

$$\zeta_{nl} = \text{const. } Z \int_0^\infty r^{-3} R^2(nl)\, dr$$

the main contribution to ζ comes from regions of small r. This implies that the screening of the magnetic electrons by the electronic contribution from the ligand lone pairs is rather efficient *overall*, and it is at least consistent to regard this screening as resulting from charge transfer from σ bonding electrons in orbitals of the conventional d^2sp^3 type. Orgel [13] has commented on the fact that 4*s*- and 4*p*-electrons do not shield 3*d*-electrons in a complex, on the grounds that in a free ion the intervals between terms arising from the d^n, d^ns, and s^ns^2 configurations show only slight changes as the charge decreases, but

[13] Orgel, *J. Chem. Phys.*, 1955, **23**, 1004.

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it must be that the twelve σ electrons contribute by force of numbers what they cannot do by virtue of their supposedly poor penetration.

Owen's procedure [1] amounts to a simple charge renormalisation of the *d* orbital to some fraction of unity (α^2) to account for the amount of the electrons lost to the ligand orbitals [the fraction being 0·87 for Ni(II), 0·79 for V(II), 0·62 for V(III), and 0·63 for Cr(III)]. The assumption is made that the d_ϵ shell is essentially unaffected by the d_γ* electron delocalisation,[14] and this seems to be true if considered only in the light that the d_ϵ functions have nodes along the line of the metal–ligand directions. However, another important factor affecting the d_ϵ shell would be any change in the central force field in which they move, and this will certainly be modified by such charge transfer as may occur even in the Owen model.

It thus seems difficult to assume that the spin–orbit coupling of a bound ion should be even nearly the same as that for the free ion; so this does not permit α^2 to be interpreted in such a simple manner. The equivalence of λ for free and bound ions requires, on a crystal-field picture, that the stabilisation of the d_ϵ shell relatively to the d_γ shell is exactly offset by the destabilisation of the whole $d_\epsilon d_\gamma$ set by the spherical term in the expansion of the perturbation potential in spherical harmonics. This is unlikely except in very special circumstances.

Support for the change in the spin–orbit coupling constant for the bound ion comes from Brown's work; [15] he pointed out that in the spectrum of ruby [*i.e.*, Cr(III) with O^{2-} as anion] the two transitions $^2E_{2g} \leftarrow {}^4A_{2g}$ and $^2T_{2g} \leftarrow {}^4A_{2g}$ are separated by the interval $6B + 10F_4$ which has the value about 12,000 cm.$^{-1}$ in the free ion, whereas the value found in the ruby spectrum is about 7000 cm.$^{-1}$. These transitions are configurationally wholly t_{2g}, so that it appears that the potential, in so far as it affects the t_{2g}-electrons, has suffered a drastic reduction.

On the other hand, allowing charge transfer to occur so that the net charge on the central ion is never greater than unity allows d_ϵ and d_γ orbital expansion, so that overlap and subsequent delocalisation of both $d\sigma$ and $d\pi$ type may more readily occur.

The following further evidence also supports the foregoing conclusion.

(3) *Energetic Considerations.*—From a simple consideration of the ionisation potential of metal ions [3] and ligands it is possible to strengthen the above conclusions. The Figure shows a simple energy (not free-energy) diagram for the system H_2O–Fe. It emphasises the small difference in energy between Fe^{2+}–H_2O^+ and Fe^+–$2(H_2O^+)$ compared with the other possible canonical structures. The first-row transition elements all have similar features since their ionisation potentials are of the same order. In fact the central ion has only to take one-sixth of its total electronic requirements from each ligand molecule and this will further favour the Fe^+–$2(H_2O^+)$ and Fe–$3(H_2O^+)$ structures over the other possible ones if the ligands are supposed to be within the distance where hyperpolarisability may set in.[16] The existence of such a marked energy minimum for the Fe^+–$2(H_2O^+)$ system can thus be taken as further justification for regarding charge transfer as real in such molecules.

Conclusion.—The three independent sources of data agree not only with the concept of charge transfer but also approximately with its extent. The decrease in the one-electron spin–orbit parameters may be ascribed to a mixture of a decreased central field potential due to increased screening by the donated σ electrons and the *resulting* decreased effective potential field due to the antibonding nature of the d_γ* orbital so formed. Certainly it is physically impossible, once the final "equilibrium" between ligands and central ion is established, to separate the effects into components, but on the evidence presented it seems helpful to regard the charge transfer as the dominant feature.

The energetics alone suggests that charge transfer is unavoidable, at least to the extent

[14] Bleaney, Bowers, and Pryce, *Proc. Roy. Soc.*, 1955, *A*, **228**, 166.
[15] Brown, *J. Chem. Phys.*, 1958, **28**, 67.
[16] Coulson, Maccoll, and Sutton, *Trans. Faraday Soc.*, 1952, **48**, 106.

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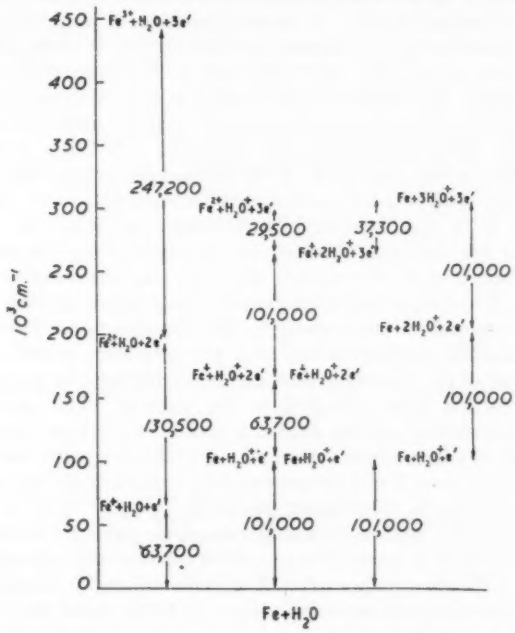
of one electron for a tripositive hydrate complex, and that the situation is at least favourable towards a further one-electron transfer for complexes of both di- and tri-positive ions.



It is concluded, therefore, that the Pauling electroneutrality principle appears to be strongly supported upon both experimental and theoretical grounds.

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126. *The Reducing Action of Glycols in Alkali. Part II.*[1]

By Wadie Tadros, Moheb Sadek Ishak, and Edward Bassili.

Nitro-aromatic compounds are reduced by sodium 2-hydroxyethoxide in ethylene glycol to give the azo-compounds but, according to conditions, azoxy-compounds may be formed in addition and are, in fact, intermediate products. In the presence of a *para*-halogen atom, an ether or the azo- and azoxy-compound or a mixture may be obtained depending on the concentration of alkali.

Aromatic nitro-compounds are readily reduced by sodium 2-hydroxyethoxide in ethylene glycol, which had been shown [1] to convert substituted benzaldehydes into the corresponding stilbenes, alcohols, and acids. The glycol appears to be oxidised in the process.[2] Nitrobenzene was readily reduced by sodium 2-hydroxyethoxide in ethylene glycol, the

[1] Part I, Tadros, Ekladius, and Sakla, *J.*, 1954, 2351.
[2] Fry and Bowman, *J. Amer. Chem. Soc.*, 1930, **52**, 1531; B.P. 271818/9 (*Brit. Abs.*, 1928, 360), see Simons and Ratner, *J.*, 1944, 421.

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reaction being vigorous. The main product was azobenzene, but some azoxybenzene was also produced according to the concentration of the reagent. The azobenzene was composed almost exclusively of the *trans*-isomer, the *cis*-isomer being formed only in traces, if at all (tested as by Badger *et al.*[3]). If formed however, it would be converted into the *trans*-isomer at the temperature of reaction (see Hartley [4]). With *p*-chloro- and *p*-bromonitrobenzene, the course of reaction was influenced by the concentration and the relative quantity of the reagent: (A) When the alkalinity was low, with one mol. of reagent, the main product was *p*-2-hydroxyethoxynitrobenzene, a small quantity of both the azoxy- and the azo-halogen compounds being also formed. (B) With a more concentrated solution or with 2 mol. of the reagent, 4 : 4′-dichloro(or dibromo)-azoxy- and -azo-benzene were formed, together with *p*-2-hydroxyethoxynitrobenzene; with 2 mol. of reagent a small quantity of 4 : 4′-di-2″-hydroxyethoxyazobenzene was also formed. Brand [5] similarly noted that the product obtained on treatment of *o*-chloronitrobenzene with alcoholic alkoxide varied with the alcohol and with the concentration of the reagent. The formation of *p*-2-hydroxyethoxynitrobenzene was evidently due to the activation induced by the presence of the nitro-group in the *para*-position. On the other hand, in conditions (B) the alkaline medium would alter the activating power of the nitro-group, probably with reversal of the electronic shift and hence the relative increase of the electron density round the carbon atom attached to the halogen. This would hinder the S_N reaction, but would evidently aid the oxidising power of the nitro-group, leading to the formation of the azoxy- and azo-compounds. Interference with the activating nitro-substituent by the alkali, even if not accompanied by reduction, should be borne in mind in interpreting results for the S_N mechanism involved.

Reduction of *m*-chloro- and *m*-bromo-nitrobenzene gave the corresponding azoxy-compounds which on further heating were converted into the azo-compounds. *o*- and *m*-Nitrotoluene gave the azo-compounds. A number of azoxy-compounds were readily converted into the corresponding azo-compounds. *p*-Nitrotoluene reacted very vigorously and the main product consisted of an orange-red substance which was sparingly soluble in most organic solvents (cf. products obtained by Fischer and Hepp,[6] Green, Davies, and Horsfall [7]).

Experimental

4 : 4′-*Dichloroazoxybenzene*.—This was prepared by a modification of the method used in the preparation of azoxybenzene.[8] *p*-Chloronitrobenzene (27 g.), dextrose (42 g.), and sodium hydroxide (30 g.) in water (100 c.c.) were heated to the b. p. for 5 hr., then diluted with water and steam-distilled. The product was filtered off, and recrystallised from acetic acid to give 4 : 4′-dichloroazoxybenzene (8 g.), m. p. and mixed m. p. with an authentic sample (prepared by Willgerodt's method [9]) 153—154°.

Reactions with Sodium 2-Hydroxyethoxide in Ethylene Glycol.—(*a*) *With anisaldehyde*. In repetition of the experiment previously reported,[1] but the solution being refluxed for 3—5 min. instead of 3·5—4 hr., the same products were obtained.

(*b*) *With nitro-compounds*. The reaction was vigorous. The nitro-compound and sodium 2-hydroxyethoxide in ethylene glycol were heated for a short time at the b. p., then diluted with water and steam-distilled. With nitrobenzene the main part of the azobenzene was also allowed to steam-distil. The alkaline solution was cooled and filtered, and the product was recrystallised or fractionated if it were a mixture. The products (Table; action of *p*-chloro- and *p*-bromo-nitrobenzene not included) were identified by analysis or mixed m. p. with an authentic sample. Azoxy- and azo-compounds were usually orange-red or reddish-brown.

[3] Badger, Buttery, and Lewis, *J.*, 1953, 2143.
[4] Hartley, *J.*, 1938, 633.
[5] Brand, *J. prakt. Chem.*, 1903, **67**, 145.
[6] Fischer and Hepp, *Ber.*, 1893, **26**, 2231.
[7] Green, Davies, and Horsfall, *J.*, 1907, 2076.
[8] Vogel, "A Text Book of Practical Organic Chemistry," Longmans, Green and Co., London, 1st Edn., 1948, p. 604.
[9] Willgerodt, *Ber.*, 1882, **15**, 1002.

(*c*) *Reaction with azoxy-compounds.* The azo-compounds obtained were recrystallised and identified as in (*b*) (Table).

Reduction of nitro-compounds $X \cdot C_6H_4 \cdot NO_2$

X	Nitro-cpd. (mol.)	Sodium (g.-atom)	Ethylene glycol (c.c.)	Heating (min.)	Solv.	Products: azo (g.; m. p.)	Products: azoxy (g.; m. p.)
H	0·1	0·1	25	2—3	P	1·5; 67—68° [a]	6·5; 36°
,,	,,	,,	50	5	P	5·4; 67—68	
,,	,,	,,	,,	20	P	6·5; 67—68	
,,	,,	,,	,,	75	P	6·7; 67—68	
,,	,,	,,	,,	90	P	6·7; 67—68	
,,	,,	0·2	100	3—5	P	8·0; 67—68	
o-Me	,,	0·1	50	5	E	2·0; 51	
	,,	,,	,,	15	E	3·0; 51	
m-Me	,,	,,	,,	60	A	8·5; 51 [b]	
o-Cl	,,	,,	,,	2	P	0·1; 136 [c]	
m-Cl	,,	,,	,,	3—5	A	—	13·0; 95—96 [d]
	0·05	,,	,,	20—25	A	4·9; 101 [e]	
m-Br	0·1	,,	,,	2	A	—	17·4; 110—111
	0·05	,,	,,	10—15	A	7·0; 125	
p-HO·CH_2·CH_2·O	0·1	,,	,,	3—5	A	3·0; 200 [f]	

Reduction of azoxy-compounds $X \cdot C_6H_4 \cdot N(O) \cdot N \cdot C_6H_4 \cdot X$

H	0·05	0·1	50	3—5	P	8·0; 67—68	
2-Me	,,	,,	,,	3—5	E	10·0; 53—54	
4-Cl	,,	,,	,,	3—5	An or Ac	9·6; 184—185° [g]	

Solvents: A = alcohol; Ac = acetic acid; An = acetone; E = ether; P = light petroleum (b. p. 50—70°). [a] Found: C, 78·5; H, 5·4; N, 15·4. Calc. for $C_{12}H_{10}N_2$: C, 79·1; H, 5·5; N, 15·4%. [b] Found: C, 79·9; H, 6·7; N, 13·0. Calc. for $C_{14}H_{14}N_2$: C, 80·0; H, 6·7; N, 13·3%. Goldschmidt (*Ber.*, 1878, **11**, 1624) also gave m. p. 51°; others gave 54—55°. [c] Found: C, 57·0; H, 3·3; N, 11·0. Calc. for $C_{12}H_8N_2Cl_2$: C, 57·4; H, 3·2; N, 11·2%. [d] Found: N, 10·0; Cl, 26·2. Calc. for $C_{12}H_8ON_2Cl_2$: N, 10·5; Cl, 26·6%. [e] Found: C, 57·2; H, 3·4; N, 11·0; Cl, 28·5. Calc. for $C_{12}H_8N_2Cl_2$: C, 57·4; H, 3·2; N, 11·2; Cl, 28·3%. [f] Found: C, 40·9; H, 2·3; N, 7·4; Br, 44·7. Calc. for $C_{12}H_8ON_2Br_2$: C, 40·4; H, 2·2; N, 7·9; Br, 44·9%. [g] Found: C, 63·5; H, 5·9; N, 9·5. $C_{16}H_{18}O_4N_2$ requires C, 63·6; H, 6·0; N, 9·3%. [h] Found: C, 57·2; H, 3·3; N, 11·0; Cl, 28·0. Calc. for $C_{12}H_8N_2Cl_2$: C, 57·4; H, 3·2; N, 11·2; Cl, 28·3%.

Reduction of Nitrobenzene by the Sodium Derivative of Propylene Glycol.—Nitrobenzene (12·3 g.) and the sodium derivative (2·3 g.) in propylene glycol (50 c.c.) were heated at the b. p. for 3—5 min., then diluted with water and steam-distilled. Azobenzene (8·2 g.) passed over, and on recrystallisation from alcohol or light petroleum (b. p. 50—70°) formed orange-red crystals, m. p. and mixed m. p. 67—68°.

Influence of Concentration and Proportion of Reagent on the Course of the Reaction with p-*Halogeno-nitrobenzenes.* (A) (1). A solution of sodium hydroxide (4 g., 0·1 mol.) in water (10 c.c.) was added dropwise to a boiling solution of *p*-chloronitrobenzene (15·8 g., 0·1 mol.) in ethylene glycol (50 c.c.) with stirring, boiling being continued for a further 5 min. after complete addition. The colour of the solution changed to pale orange, red, and finally dark red. The product was diluted with water and steam-distilled to remove unchanged *p*-chloronitrobenzene (2·25 g.). The alkaline solution was filtered while hot, and the residue recrystallised from alcohol or acetic acid to give 4 : 4′-dichloroazoxybenzene (0·85 g.), m. p. and mixed m. p. 154—155°. The alkaline filtrate gave on cooling and further concentration *p*-2-hydroxyethoxynitrobenzene which recrystallised from water as crystals (overall yield, 9·9 g.), m. p. 83—84° (Found: C, 52·5; H, 4·9; N, 7·7. Calc. for $C_8H_9O_4N$: C, 52·5; H, 4·9; N, 7·7%). (2) A solution of sodium 2-hydroxyethoxide (from 2·3 g. of sodium; 0·1 g.-atom) in ethylene glycol (25 c.c.) was added dropwise to a boiling solution of *p*-chloronitrobenzene (15·8 g.; 0·1 mol.) in ethylene glycol (25 c.c.) as above. Steam-distillation gave unchanged material (1·5 g.). The residue was filtered off and treated with the minimum of hot alcohol. 4 : 4′-Dichloroazoxybenzene (0·75 g.), m. p. and mixed m. p. 154—155°, separated. The alcohol-insoluble fraction was recrystallised from acetone to give 4 : 4′-dichloroazobenzene (1·2 g.) as brownish-yellow crystals, m. p. and mixed m. p. 185°. The alkaline filtrate gave on cooling and concentration *p*-2-hydroxyethoxynitrobenzene (overall yield, 8·7 g.). (3) A relatively dilute solution of *p*-chloronitrobenzene (15·8 g.; 0·1 mol.) in a solution of sodium 2-hydroxyethoxide (from

2·3 g. of sodium; 0·1 g.-atom) in ethylene glycol (100 c.c.) was refluxed for 3—5 min., and the product was treated as above (unchanged *p*-chloronitrobenzene, 0·8 g.; 4 : 4′-dichloroazobenzene, 1·2 g.; and *p*-2-hydroxyethoxynitrobenzene, 12·0 g., were obtained).

(B) (i) When only 50 c.c. of ethylene glycol were used in experiment (A, 3) above, unchanged *p*-chloronitrobenzene (0·82 g.), 4 : 4′-dichloroazobenzene (3·73 g.), and *p*-2-hydroxyethoxynitrobenzene (5·54 g.) were obtained. (ii) Under similar conditions *p*-bromonitrobenzene (20·2 g.; 0·1 mol.) afforded unchanged *p*-bromonitrobenzene (0·2 g.), 4 : 4′-dibromoazobenzene [6·0 g.; orange-red crystals from benzene, m. p. 205° (Found: C, 42·4; H, 2·4; N, 8·0; Br, 46·2. Calc. for $C_{12}H_8N_2Br_2$: C, 42·4; H, 2·4; N, 8·2; Br, 47·1%)], and *p*-2-hydroxyethoxynitrobenzene (5·0 g.). (iii) Repetition of experiment (A, 3) but with 4·6 g. of sodium, gave *p*-chloronitrobenzene (0·05 g.), recovered by steam-distillation, and the residue obtained on cooling the alkaline solution was filtered off and washed with little acetone. Recrystallisation of the residue from acetone gave 4 : 4′-dichloroazobenzene (3·6 g.). The acetone mother-liquor was evaporated to dryness, and the residue treated with hot benzene. The insoluble fraction was recrystallised from alcohol, 4 : 4′-dihydroxyethoxyazobenzene (0·55 g.) separating as golden-yellow crystals, m. p. and mixed m. p. 200°. The benzene mother-liquor gave on cooling a yellow substance (0·95 g.), m. p. 145°, which is being investigated.

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127. *Steroids and Walden Inversion. Part XLII.* 5α-Cholestan-4-one and Some Derivatives thereof.*

By C. W. SHOPPEE, M. E. H. HOWDEN, R. W. KILLICK, and G. H. R. SUMMERS.

5α-Cholestan-4-one is readily obtained from cholest-4-ene by rearrangement of the derived 4α : 5α-epoxide to 5β-cholestan-4-one and isomerisation of the latter. The 4β : 5β-epoxide has been prepared and by rearrangement gives 5α-cholestan-4-one.

Bromination of the 5-epimeric cholestan-4-ones affords the same 5-bromo-5α-cholestan-4-one, which in the presence of hydrogen bromide affords 3α-bromo-5α-cholestan-4-one, also obtained by the action of hydrogen bromide on 5-hydroxy-5α-cholestan-4-one. Dibromination of 5α-cholestan-4-one gives 3α : 5-dibromo-5α-cholestan-4-one.

THE general symmetry of the steroid 4- and 6-positions suggested that recent studies on 5α-cholestan-6-one [1] and the epimeric 5α-cholestan-6-ols [2] should be paralleled by work on 5α-cholestan-4-one and related compounds.

Although 5α-cholestan-4-one (X) was prepared some forty years ago by Windaus [3] from cholest-4-ene (I) by nitration and reduction of the resulting 4-nitrocholest-4-ene with zinc and acetic acid, the yield is poor and the product contaminated with cholest-4-en-3-one and cholest-4-en-6-one. Thus the ketone (X) and its derivatives have been relatively inaccessible and little investigated,[4,5] and we have devised a new and convenient method of preparation.

Cholest-4-ene (I) by treatment with perbenzoic acid gives the 4α : 5α-epoxide (II),[6,7] whose structure follows from its acetolysis [6] to the 4-monoacetate [5,8] of 5α-cholestane-4β : 5-diol (III) and its catalytic hydrogenation [6,7] to a mixture of 5α-cholestan-4α-ol [4,5] (V)

* Part XLI, *J.*, 1959, 345.

[1] Shoppee, Jenkins, and Summers, *J.*, 1958, 1657.
[2] Shoppee and Summers, *J.*, 1952, **3361**; Shoppee and Howden, *Chem. and Ind.*, 1958, 414.
[3] Windaus, *Ber.*, 1920, **53**, 488.
[4] Tschesche and Hagedorn, *Ber.*, 1935, **68**, 2251; Barton and Rosenfelder, *J.*, 1951, 1048.
[5] Shoppee, D. N. Jones, Lewis, and Summers, *J.*, 1955, 2876.
[6] Heilbron, Shaw, and Spring, *Rec. Trav. chim.*, 1933, **57**, 529.
[7] Plattner, Petrzilka, and Lang, *Helv. Chim. Acta*, 1944, **27**, 523.
[8] Bergmann and Skau, *J. Org. Chem.*, 1940, **5**, 439.

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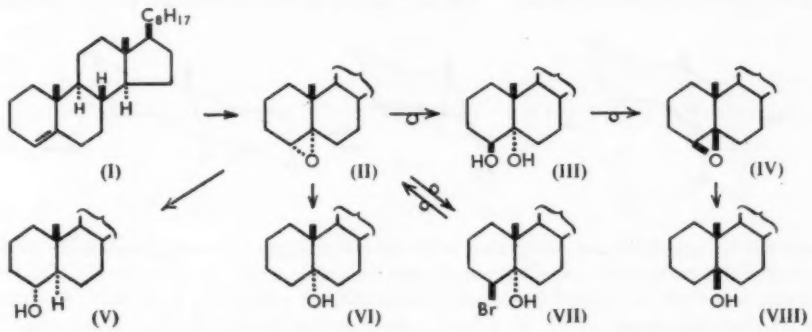
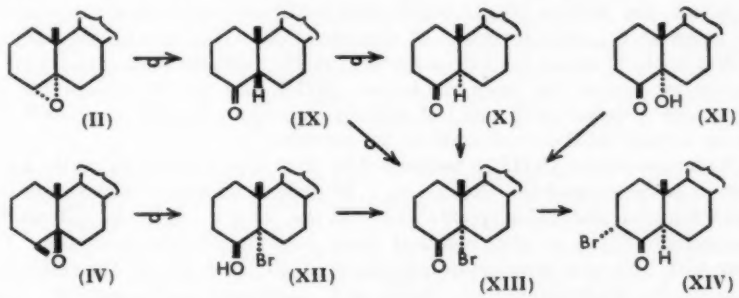
and -5-ol [7,9] (VI). The 4α : 5α-epoxide (II) resists reduction with lithium aluminium hydride in ether at 35°, but is smoothly converted in refluxing dioxan into 5α-cholestan-5-ol (VI) (Henbest and Wilson [10] state that the 4α : 5α-epoxide is reduced with this hydride to 5α-cholestan-5-ol but give no experimental details), and by diaxial fission with hydrogen bromide gives the 4β-bromo-5α-alcohol (VII), partially reconverted into the epoxide by treatment with aluminium oxide.



The 4β : 5β-epoxide (IV) is readily prepared from the diacetate [5] of 5α-cholestane-4β : 5-diol (III) by treatment with hot ethanolic potassium hydroxide; it is reduced by lithium aluminium hydride in ether at 36°, presumably by bimolecular substitution [11] [S_N2] with inversion of configuration at $C_{(4)}$, and so with diaxial fission, to 5β-cholestan-5-ol (VIII) in nearly quantitative yield.

Pinacolic rearrangement of substituted ethylene oxides to ketones can be accomplished by use of acids [12] or electrophilic reagents such as boron trifluoride [13,14] or ferric chloride.[13] Thus the 4α : 5α-epoxide (II) is rearranged by brief treatment with boron trifluoride with inversion of configuration at the migration terminus to give 5β-cholestan-4-one [15] (IX),

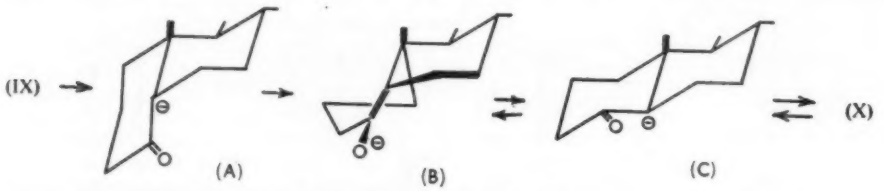


readily isomerised by treatment with acid, alkali, or aluminium oxide [5] to the more thermodynamically stable 5α-cholestan-4-one (X). Since this work was done, the same reaction sequence (II ⟶ IX ⟶ X) has been described independently by Henbest and Wrigley.[16]

[9] Fudge, Shoppee, and Summers, *J.*, 1954, 958.
[10] Henbest and Wilson, *J.*, 1957, 1960.
[11] Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 2149, 2152.
[12] Lagrave, *Ann. Chim.* (*France*), 1927, **8**, 363.
[13] Heusser, Eichenberger, Kurath, Dällenbach, and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106; Heusser, Anliker, Eichenberger, and Jeger, *ibid.*, 1952, **35**, 936.
[14] Heusler and Wettstein, *Helv. Chim. Acta*, 1953, **36**, 398; Bladon, Henbest, E. R. H. Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.
[15] Stevenson and Fieser, *J. Amer. Chem. Soc.*, 1956, **78**, 1409.
[16] Henbest and Wrigley, *J.*, 1957, 4596.

XUM

Monobromination in acetic acid containing a trace of hydrogen bromide at 20° of either 5β- or 5α-cholestan-4-one (IX or X) gives the same 5-bromo-5α-cholestan-4-one (XIII), $[\alpha]_D$ +66°, whose ultraviolet and infrared absorption spectra ($\Delta\lambda_{max.}$ +25 mμ, log ε +0·4; $\Delta\nu_{max.}$ 0) demonstrate the uniquely axial character of the bromine atom. Corey [17] has suggested that axial bromides are the initial products of bromination of ketones; replacement of the axial 5-hydrogen atoms in the ketones (IX) and (X) might therefore appear to lead to epimeric 5-bromo-ketones. The mechanism of the bromination process, however,



permits the energy difference associated with the *cis*- and *trans*-A/B-ring fusions to operate; if we write the carbanions (A, C) theoretically derivable from the ketones (IX, X), then the enolic anion (B) is formed irreversibly from (A) but reversibly from (C). Formation from 5β-cholestan-4-one (IX) of 5-bromo-5α-cholestan-4-one (XIII) shows that the reaction is thermodynamically controlled, and provides a further example of the generalisation that carbanion reductions (protonation,[18] carboxylation,[19] bromination) yield the more thermodynamically stable product.

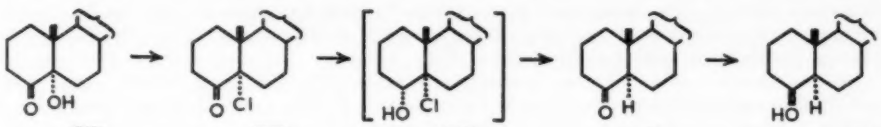
Reduction of the 5α-bromo-ketone (XIII) with sodium borohydride in methanol at 20° yielded a non-crystalline product containing little, if any, of the 5α-bromo-4β-alcohol (XII) and consisting largely or exclusively of the epimeric 5α-bromo-4α-alcohol, since treatment with hot methanolic potassium hydroxide gave a good yield of 5α-cholestan-4-one (X), unaccompanied by the 4β : 5β-epoxide (IV). The crystalline 5α-bromo-4β-alcohol (XII) is obtained from the 4β : 5β-epoxide (IV) by diaxial fission with hydrogen bromide at 20°; the reaction appears to involve protonation, to furnish the conjugate acid of the 4β : 5β-epoxide, the positive pole of which then facilitates bimolecular substitution by a bromine anion at $C_{(5)}$ with inversion of configuration. Oxidation of the 5α-bromo-4β-alcohol (XII) with chromium trioxide–acetic acid at 20° yields the 5α-bromo-ketone (XIII). An attempt to convert the 5α-bromo-ketone (XIII) into the 4β : 5β-epoxide (IV) by treatment with a deficit (0·25 mol.) of lithium aluminium hydride in ether [16,20] failed, possibly on account of the small scale of the experiment.

The 5α-bromo-ketone (XIII) is isomerised by hydrogen bromide in acetic acid at 20° to 3α-bromo-5α-cholestan-4-one (XIV), $[\alpha]_D$ −78°, whose structure follows from its ultraviolet and infrared absorption spectra ($\Delta\lambda$ +25 mμ, Δlog ε +0·4; $\Delta\nu$ +3 cm.$^{-1}$). The 3α-bromo-ketone (XIV) is also obtained from 5-hydroxy-5α-cholestan-4-one (XI) by treatment with hydrogen bromide in chloroform at 20°, probably as the result of initial formation of the 5α-bromo-ketone (XIII) and subsequent rearrangement. Both the 5α- (XIII) and the 3α-bromo-ketone (XIV) on reduction with zinc–acetic acid regenerate the parent ketone (X).

5-Hydroxy-5α-cholestan-4-one (XI) on treatment with hydrogen chloride in chloroform at 20° furnished a chloro-ketone, which we regard as 5-chloro-5α-cholestan-4-one (XV; Cl, axial) by analogy with the conversion with hydrogen chloride of 5-hydroxy-5α-cholestan-6-one into 5-chloro-5α-cholestan-6-one,[1] and because the hydrogen halides are incapable of causing rearrangement of α-chloro-ketones, *e.g.*, (XV) ⟶ (XIV with Cl for Br).[21] The

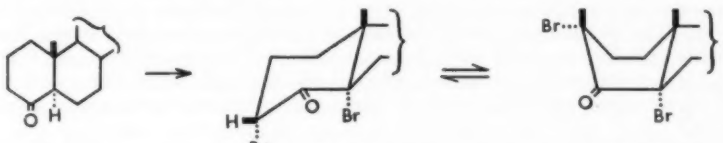
[17] Corey, *J. Amer. Chem. Soc.*, 1953, **75**, 2301; 1954, **76**, 175.
[18] Barton, *Experientia*, 1955, **11**, Suppl. II, 121; Barton and Robinson, *J.*, 1954, 3045.
[19] Roberts and Shoppee, *J.*, 1954, 3418.
[20] E. R. H. Jones, Henbest, Wagland, and Wrigley, *J.*, 1955, 2477.
[21] Ellis and Petrow, *J.*, 1953, 3869; Beereboom and Djerassi, *J. Org. Chem.*, 1954, **19**, 1196.

infrared carbonyl absorption maximum of (XV) shows a displacement of 9 cm.$^{-1}$, compared with that of 4 cm.$^{-1}$ for 5-chloro-5α-cholestan-6-one,[1,22] for which we cannot account;



(XI) (XV) (XVI) (X) (XVII)

however, the ultraviolet absorption is consistent with formula (XV). The chloro-ketone is reduced by sodium borohydride in methanol at 20° to a mixture of 5α-cholestan-4-one



(X) (XIXA) (XIXB)

(X) and -4β-ol (XVII). The ketone may be formed by the easy dehydrochlorination of an intermediate 5α-chloro-4α-alcohol (XVI), or may result from removal of chlorine by attack of BH_4^- on the halogen of the 5α-chloro-ketone [20] to give initially the carbanion (C), of 5α-cholestan-4-one (X). The alcohol is produced by further reduction of the ketone (X), which with lithium aluminium hydride in ether at 15° gives 90% of the 4β-alcohol (XVII) accompanied by 7% of the 4α-alcohol.[5]

[*Amended, October 29th*, 1958.] Dibromination of 5α-cholestan-4-one (X) in acetic acid at 20° gave a dibromo-ketone, reduced by zinc and ethanol to the parent ketone, which we regard as 3α : 5-dibromo-5α-cholestan-4-one (XIX). The carbonyl absorption band was composed of two maxima at 1709 and 1722 cm.$^{-1}$ of nearly equal intensity, which could not completely be resolved. Allinger and Allinger [24] have recently described curves of similar contour for the carbonyl absorption of 2-bromo*cyclo*hexanone; they attribute the twin peaks to an equilibrium in solution of the two (chair) conformational isomers [$\nu_{max.}$ 1742 (bromine equatorial), 1730 (bromine axial); cf. *cyclo*hexanone, $\nu_{max.}$ 1730 cm.$^{-1}$; both in carbon tetrachloride]. We suggest that the 3α : 5α-dibromo-ketone (XIX) exists in solution as an equilibrium mixture of the chair conformation (XIXA) and the boat conformation (XIXB).

Since axial α-bromine atoms do not affect the frequency of the adjacent carbonyl absorption maximum, structure (XIXA) should absorb at ~1712 cm.$^{-1}$ [$\Delta\nu$ −3 cm.$^{-1}$; cf. 5 : 7α-dibromo-5α-cholestan-6-one [1] ($\Delta\nu$ +2 cm.$^{-1}$) and its 3β-acetoxy-derivative [25] ($\Delta\nu$ −3 cm.$^{-1}$)]; a boat-equatorial α-bromine atom increases the frequency of the adjacent carbonyl absorption maximum,[26] so that structure (XIXB) should absorb at ~1722 cm.$^{-1}$ [$\Delta\nu$ +10 cm.$^{-1}$]. The ultraviolet absorption spectrum of (XIX) showed a maximum at 312 mμ, log ε 2·1 [(XIXB) bromine axial: $\Delta\lambda$ +27 mμ, Δ log ε +0·6] with some indication of a point of inflexion at ~340 mμ [(XIXA) : 2 bromine atoms diaxial : $\Delta\lambda$ ~+55 mμ].

The existence of an equilibrium (XIXA ⇌ XIXB) may reasonably be attributed to reduction of the large steric repulsion of the diaxial 3α- and 5α-bromine atoms in (XIXA) at the expense of some increase of dipolar repulsion between the equatorial 3α-bromine–carbon bond and the 4-carbonyl group and of the steric repulsion of the 3β-hydrogen atom and the 10β-methyl group in (XIXB).

[22] Cummins and Page, *J.*, 1957, 3847.
[23] Henbest and Hallsworth, *J.*, 1957, 4604.
[24] Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.
[25] Cookson, *J.*, 1954, 282.
[26] Barton, Lewis, and McGhie, *J.*, 1957, 2907.

XUM

Experimental

For general experimental directions see *J.*, 1959, 345. $[\alpha]_D$ are in $CHCl_3$; ultraviolet absorption spectra were determined on a Hilger Uvispek spectrophotometer in EtOH and infrared absorption spectra on a Perkin-Elmer Model 21 double-beam instrument, or a Grubb-Parsons double-beam grating instrument, in CCl_4.

5α-Cholestan-5-ol.—4α : 5-Epoxy-5α-cholestane [m. p. 100—101° (from ethanol), $[\alpha]_D$ +80° (*c* 1·1)] (235 mg.) in dioxan (30 c.c.) was refluxed with lithium aluminium hydride (200 mg.) for 4 hr. The usual isolation procedure gave 5α-cholestan-5-ol (158 mg., 68%), m. p. 106—108°, $[\alpha]_D$ +12° (*c* 1·8), $\nu_{max.}$ 3605 cm.$^{-1}$ (OH), after two crystallisations from aqueous acetone [Found: (after drying at 50°/0·5 mm. for 48 hr.): C, 83·5; H, 12·4. Calc. for $C_{27}H_{48}O$: C, 83·4; H, 12·4%].

4β-Bromo-5α-cholestan-5-ol.—4α : 5-Epoxy-5α-cholestane (246 mg.) in acetic acid (5 c.c.) and a little ether was treated with a 2% solution of hydrogen bromide in acetic acid (7·5 c.c.) at 20° for 2 hr. The solution was poured into sodium hydrogen carbonate solution, and worked up to give the *4β-bromo-5α-alcohol* (270 mg.), m. p. 108° [Found: Br, 17·0. $C_{27}H_{47}OBr$ requires Br, 17·1%], which decomposed on attempted crystallisation from ethanol or acetone. Chromatography on alkaline aluminium oxide gave some 4α : 5-epoxy-5α-cholestane, m. p. and mixed m. p. 97—99°.

4β : 5-Epoxy-5β-cholestane.—5α-Cholestane-4β : 5α-diol diacetate (m. p. 157—158°, cf. lit.,[8] 147—148°; 1·6 g.) in ethanol (80 c.c.) was refluxed with potassium hydroxide (2 g.) for 2·5 hr. The usual isolation procedure gave a yellow oil, whose pentane solution by filtration through deactivated aluminium oxide and evaporation, and crystallisation from ether–methanol gave *4β : 5-epoxy-5β-cholestane*, m. p. 60—62°, $[\alpha]_D$ +3·5° (*c* 1·45) [Found (after drying at 20°/0·02 mm. for 2 hr.): C, 84·0; H, 11·9. $C_{27}H_{46}O$ requires C, 83·9; H, 12·0%].

5β-Cholestan-5-ol.—4β : 5-Epoxy-5β-cholestane (200 mg.) was refluxed in ether with excess of lithium aluminium hydride for 0·5 hr. The usual isolation procedure gave an oil, which was chromatographed on a column of aluminium oxide (6 g.) prepared in pentane. Elution with ether gave a colourless oil (180 mg.), which by crystallisation from pentane and recrystallisation from methanol gave 5β-cholestan-5-ol, m. p. 82—84°, $[\alpha]_D$ +35° (*c* 0·9) (lit.,[23] m. p. 81—82°, $[\alpha]_D$ +37°).

5-Bromo-5α-cholestan-4β-ol.—4β : 5-Epoxy-5β-cholestane (350 mg.) in acetic acid (6 c.c.) and a little ether was treated with a 2% solution of hydrogen bromide in acetic acid (8 c.c.) at 20° for 2 hr. The crystalline product was filtered off, dried, and recrystallised from acetone, to afford *5-bromo-5α-cholestan-4β-ol*, m. p. 104—106°, $[\alpha]_D$ +40° (*c* 0·8) [Found (after drying at 20°/0·02 mm. for 2 hr.): C, 69·3; H, 10·1. $C_{27}H_{47}OBr$ requires C, 69·35; H, 10·1%].

5β-Cholestan-4-one.—4α : 5-Epoxy-5α-cholestane (300 mg.; dried by azeotropic distillation with benzene at 10 mm.) in benzene (15 c.c.) was treated with a solution of boron trifluoride–ether complex (0·3 c.c.) in benzene at 20° for 3 min. After addition of ice-cold sodium hydrogen carbonate solution, the benzene solution was separated, washed with water, dried, and evaporated at 10 mm. to yield 5β-cholestan-4-one (150 mg.), m. p. 109°, $[\alpha]_D$ +40° (*c* 1·0), after recrystallisation from acetone (lit.,[15,23] m. p. 109—110°, 108—110°, $[\alpha]_D$ +40·5°, +38°, +44°).

5α-Cholestan-4-one.—(*a*) 4β : 5-Epoxy-5β-cholestane (100 mg.), on brief treatment in benzene with boron trifluoride–ether as above, gave 5α-cholestan-4-one (60 mg.), m. p. and mixed m. p. 96—98° (from acetone).

(*b*) 5β-Cholestan-4-one [crude product from rearrangement of 4α : 5-epoxy-5α-cholestane (3 g.) with boron trifluoride–ether] was refluxed in methanol with a trace of sodium methoxide for 0·5 hr. After partial removal of methanol in a vacuum, the residue was diluted, and extracted with ether to give, after the usual working up, 5α-cholestan-4-one (1·3 g.), m. p. and mixed m. p. 96—98° with a genuine specimen prepared by Windaus's method,[3] after crystallisation from acetone. The ketone exhibited $\lambda_{max.}$ 285 mμ (log ε 1·7), $\nu_{max.}$ 1712 cm.$^{-1}$.

5-Bromo-5α-cholestan-4-one.—(*a*) 5α-Cholestan-4-one (250 mg.) in acetic acid (30 c.c.) was treated with bromine (110 mg., 1·06 mol.) in acetic acid (2 c.c.) and a few drops of a solution of hydrogen bromide in acetic acid, and kept at 20° for 0·5 hr. The colourless solution, after the usual working up and two recrystallisations from ethanol, yielded *5-bromo-5α-cholestan-4-one* (100 mg.), m. p. 143—145°, $[\alpha]_D$ +66° (*c* 1·6), $\lambda_{max.}$ 307 mμ (log ε 2·1), $\lambda_{max.}$ 1712 cm.$^{-1}$ (in $CHCl_3$, 1706 cm.$^{-1}$) [Found (after drying at 20°/1 mm. for 17 hr.): C, 69·6; H, 9·7.

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$C_{27}H_{45}OBr$ requires C, 69·6; H, 9·7%]. Another preparation had m. p. 144—147°. The material from the mother-liquor of various preparations, by chromatography on aluminium oxide (Woelm, neutral) in hexane, elution with benzene–hexane (1 : 9), and recrystallisation from ethanol, gave a polymorphic form of *5-bromo-5α-cholestan-4-one*, m. p. 125—128°, $[\alpha]_D$ +60° (*c* 1·1), $\lambda_{max.}$ 1712 cm.$^{-1}$ [Found (after drying at 20°/1 mm. for 6 hr.): C, 70·0; H, 9·6%]; elution with benzene–hexane (1 : 4 and 1 : 2) gave 5α-cholestan-4-one, m. p. and mixed m. p. 95°; elution with ether–benzene gave non-crystalline material.

(*b*) 5-Bromo-5β-cholestan-4-one (250 mg.) in acetic acid (30 c.c.) was treated dropwise with a solution of bromine (1·06 mol.) in acetic acid as under (*a*). After 0·5 hr. the solution was worked up by dilution and extraction with ether to give the 5α-bromo-ketone, m. p. and mixed m. p. 144° (from acetone).

(*c*) 5-Bromo-5α-cholestan-4β-ol (m. p. 104—106°; 100 mg.) in acetic acid (2 c.c.) was oxidised with a 2% solution of chromium trioxide in acetic acid (1·5 c.c.) at 20° for 3 hr. The crystalline product was filtered off, washed with a little acetic acid, dried briefly in a vacuum, and recrystallised from acetone or from ethanol, to give 5-bromo-5α-cholestan-4-one, m. p. ~127° after change of crystal form and partial melting at 110—114°, $[\alpha]_D$ +63° (*c* 1·1), $\nu_{max.}$ 1712 cm.$^{-1}$. In a repetition, the material which crystallised from the reaction mixture appeared to be a solvated form, m. p. <80° with partial transformation into plates, m. p. ~132°, $[\alpha]_D$ +60° (*c* 1·1), $\nu_{max.}$ 1712 cm.$^{-1}$, the infrared absorption spectrum being identical with that of the product of m. p. ~127° and that of the forms of m. p. 145° and 125° described under (*a*).

Reduction of 5-Bromo-5α-cholestan-4-one with Sodium Borohydride.—The bromo-ketone (520 mg.) in 98% methanol (30 c.c.) was treated with sodium borohydride (300 mg.) at 20° overnight. The usual isolation procedure furnished an oil (510 mg.), which was chromatographed on a column of aluminium oxide (15 g.) prepared in hexane. Elution with benzene–hexane gave halogen-free oils. Elution with benzene and ether–benzene gave halogen-containing oils, which were united (207 mg.) and refluxed with 2% methanolic potassium hydroxide for 4 hr.; the usual working up gave an oil (160 mg.), which by chromatography on aluminium oxide (5 g.) in hexane and elution with hexane (5 × 16 c.c.) gave 5α-cholestan-4-one (132 mg.), m. p. and mixed m. p. 96—98°, $\nu_{max.}$ 1713 cm.$^{-1}$.

3α-Bromo-5α-cholestan-4-one.—(*a*) 5-Bromo-5α-cholestan-4-one (123 mg.) in acetic acid (12·5 c.c.) was treated with a 50% solution of hydrogen bromide in acetic acid (2·5 c.c.) at 20° for 40 hr. After addition of water, the product was isolated with ether and chromatographed on aluminium oxide (3·5 g.) in hexane. Elution with hexane gave 3α-bromo-5α-cholestan-4-one, m. p. 115°.

(*b*) 5-Hydroxy-5α-cholestan-4-one [5] (m. p. 159°; 500 mg.) in chloroform was treated with a stream of dry hydrogen bromide at 20° for 2 hr. Next morning the dark red solution gave by the usual isolation procedure an oil, which was chromatographed on aluminium oxide (15 g.; Woelm, neutral) in pentane. Elution with pentane (2 × 50 c.c.) gave two crystalline fractions (213 mg., 27 mg.), which were united and repeatedly recrystallised from acetone, to yield *3α-bromo-5α-cholestan-4-one* (95 mg.), m. p. 117—119° (remelt 117—120°), $[\alpha]_D$ −78° (*c* 0·8), $\nu_{max.}$ 1715 cm.$^{-1}$, $\lambda_{max.}$ 309 mμ (log ε 2·0) [Found (after drying at 20°/0·05 mm. for 16 hr.): C, 69·1; H, 9·6. $C_{27}H_{45}OBr$ requires C, 69·6; H, 9·7%]. Further elution with pentane (2 × 50 c.c.) gave two oily fractions, which on reduction with zinc in acetic acid gave 5α-cholestan-4-one.

3α : 5-Dibromo-5α-cholestan-4-one.—5α-Cholestan-4-one (300 mg.) in acetic acid (30 c.c.) was treated with a solution of bromine (255 mg., 2·05 mol.) in acetic acid in the presence of a little hydrogen bromide at 20°. After 2 hr. dropwise addition of a little water gave a precipitate of needles; after 15 min. the crystals were filtered off, washed with water, and dried. Two recrystallisations from acetone gave *3α : 5-dibromo-5α-cholestan-4-one* (124 mg.), m. p. 151—154° (decomp.), $\lambda_{max.}$ 312 mμ (log ε 2·1), $\nu_{max.}$ 1710 cm.$^{-1}$ and 1720 cm.$^{-1}$ [Found (after drying at 25°/0·2 mm. for 24 hr.): C, 61·1; H, 8·6. $C_{27}H_{44}OBr_2$ requires C, 61·4; H, 8·4%]. Another preparation had m. p. 154—155°, $\nu_{max.}$ 1709 and 1722 cm.$^{-1}$.

5-Chloro-5α-cholestan-4-one.—5-Hydroxy-5α-cholestan-4-one [5] (m. p. 159°; 990 mg.) in chloroform (10 c.c.) was treated with a stream of dry hydrogen chloride at 20° for 1 hr. The dark orange solution was evaporated completely in a vacuum, to give an oil which was chromatographed on aluminium oxide (30 g.; Woelm, acid) prepared in hexane. Elution with hexane (4 × 100 c.c.) gave crystalline fractions, which were united (711 mg.) and recrystallised from acetone, to yield *5-chloro-5α-cholestan-4-one*, m. p. 136—138°, $[\alpha]_D$ +105° (*c* 1·3), $\lambda_{max.}$ 301 mμ,

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log ε 2·0, $\nu_{max.}$ 1721 cm.$^{-1}$ [Found (after drying at 20°/0·05 mm. for 16 hr.): C, 77·1; H, 10·4. $C_{27}H_{45}OCl$ requires C, 77·0; H, 10·7%]. Elution with ether and chloroform gave some starting material.

Reduction of 5-Chloro-5α-cholestan-4-one with Sodium Borohydride.—The 5α-chloro-ketone (800 mg.) in methanol (25 c.c.) and a little ether was treated with sodium borohydride (125 mg.) at 20° overnight. The usual isolation procedure gave an oil, which was chromatographed on aluminium oxide (15 g.; Woelm, neutral) prepared in hexane. Elution with hexane (3 × 50 c.c.) gave starting material (93 mg.), m. p. 136; use of benzene–hexane (1 : 4; 6 × 50 c.c.) gave material (total, 518 mg.), which crystallised from acetone–methanol to yield 5α-cholestan-4-one, m. p. and mixed m. p. 96—98°, $\nu_{max.}$ 1710 cm.$^{-1}$. Elution with benzene (2 × 50 c.c.) gave oils. Use of ether (50 c.c.) gave 5α-cholestan-4β-ol (195 mg.), m. p. 132° [lit.,[4] m. p. 132°] after crystallisation from methanol; its infrared absorption spectrum was identical with that of a genuine specimen.

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128. *Preparation and Properties of Some Poly-O-acetylglycosyl Chlorides of the "Unstable" Series.*

By W. KORYTNYK and J. A. MILLS.

Fully acetylated aldopyranoses of 1 : 2-*trans*-configuration, and acetylated aldoses of this configuration with a free hydroxyl group at the hemiacetal centre, react with aluminium chloride in cold chloroform, giving *O*-acetylglycosyl chlorides of 1 : 2-*trans*-configuration (so-called "unstable" chlorides). The reaction is successful with 4 : 6-*O*-benzylidene- and 4 : 6-*O*-ethylidene-β-D-glucopyranose triacetate, and with β-maltose octa-acetate. The stereospecificity of the reaction, criteria for the structures of the products, and conformational implications for aldopyranoses are discussed.

O-Acetylglycosyl chlorides of 1 : 2-*trans*-configuration are fairly stable. Reported mutarotations of "unstable" chlorides are apparently due to slow reaction with traces of water in solvents.

Tetra-*O*-acetyl-β-D-mannopyranosyl chloride has been obtained in small yield by reaction of β-D-mannopyranose penta-acetate with hydrogen chloride in acetyl chloride. The significance of this finding is also discussed.

IN 1953, Dr. J. Gagolski [1] found that reaction of β-D-glucopyranose penta-acetate with anhydrous aluminium chloride in cold chloroform gave a good yield of a product identical with the "β-acetochloroglucose" obtained [2] by reaction of tetra-*O*-acetyl-α-D-glucopyranosyl bromide with "active" silver chloride. A similar observation was made at about the same time by Zemplen, Mester, and Eckhart.[3] Gagolski found that one mole of aluminium chloride ($AlCl_3$) would convert up to three moles of glucose penta-acetate into acetylglucosyl chloride, that α-D-glucopyranose penta-acetate did not react under the same conditions, and that the method showed promise for the preparation of acetylglycosyl chlorides from other acetylated sugars. The more extensive study of the reaction described here has established the main details of procedure, scope, and mechanism. The mechanism deduced fits satisfactorily into the general scheme for replacement

[1] Gagolski, Ph.D. Thesis, Adelaide, 1954.
[2] Schlubach, *Ber.*, 1926, **59**, 840.
[3] Zemplen, Mester, and Eckhart, *Acta Chim. Acad. Sci. Hung.*, 1954, **4**, 73.

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reactions in cyclic reducing sugars elaborated by Lemieux and others.[4,5,6] While the work was in progress, the Ottawa group published further papers on closely related topics; our work is in general agreement with theirs, and in several respects complementary to it.

Aluminium chloride or titanium tetrachloride has been used, in refluxing chloroform, to afford "stable" isomers of acetylglycosyl chlorides from acetylated reducing sugars,[7] and titanium chloride is a powerful epimerising agent that will react under such conditions with each of a pair of anomeric sugar acetates. Other workers had also found that under milder conditions these reagents may sometimes act more selectively. With aluminium chloride in cold chloroform, β-maltose octa-acetate afforded an oily chloride different from the crystalline hepta-*O*-acetylmaltosyl chloride obtained by using more vigorous conditions.[8] The same reagent afforded epimeric chlorides from the epimeric penta-acetates of *aldehydo*-D-arabinose methyl hemiacetal.[9] Titanium tetrachloride in chloroform at 40° rapidly converted β-D-glucopyranose penta-acetate into the β-chloride, which slowly rearranged to the α-chloride; the α-penta-acetate was relatively unreactive.[10]

Treatment of a number of anomeric pairs of sugar acetates with aluminium chloride in cold chloroform under standardised conditions has now shown that the reaction has high configurational specificity, but that ring size and conformations of pyranose sugars have little effect. The fully acetylated β-D-forms of glucopyranose, galactopyranose, galactofuranose, and xylopyranose, and α-D-mannopyranose penta-acetate, all reacted readily and gave the acetylglycosyl chloride of the same configuration as the acetate used, whereas the anomeric acetate was in every case recovered unchanged (α-D-xylopyranose tetra-acetate was not available). A quantitative study of the rates for the various sugars would be difficult, and was not attempted.

The reaction constitutes a stereospecific synthesis of acetylglycosyl chlorides of 1 : 2-*trans*-configuration from sugar acetates of 1 : 2-*trans*-configuration, and therefore probably belongs to the class of reaction in which displacement of a group at position 1 depends on participation by the neighbouring 2-acetoxy-group.[4] The following mechanism is suggested: the electrophilic aluminium atom becomes co-ordinated to the ether-oxygen of the 1-acetoxy-group, and the resulting change in polarity, assisted by electron-displacement from the 2-acetoxy-group, causes transfer of the acetoxy-group from position 1 to aluminium. Complete separation of $AlCl_3{\cdot}OAc^-$ to afford the free ion (II) (which might exist in mesomeric forms) is unlikely, although an ion-pair may be transiently formed. More probably, transfer of chlorine from aluminium to position 1 within the reaction complex (I) is practically synchronous with fission of the $C_{(1)}$–acetoxyl bond. The primary products are tetra-*O*-acetyl-β-D-glucopyranosyl chloride, shown in its most stable conformation (III), and aluminium dichloride acetate. The stoicheiometry of the reaction[1] requires the latter to effect replacement in more penta-acetate, but whether it acts directly, or by disproportionation to aluminium trichloride, is not known. Stannic trichloride acetate transfers acetoxy-groups, not chlorine atoms, to β-D-glucopyranose penta-acetate.[10]

The efficiency of participation by groups other than acetate was examined. A 2-benzoyloxy-group, as in β-D-glucopyranose 1 : 3 : 4 : 6-tetra-acetate 2-benzoate, permitted normal displacement of the 1-acetoxy-group by aluminium chloride. When a 1-benzoyloxy-group was also present, in β-D-glucopyranose pentabenzoate, satisfactory reaction could not be effected even with titanium tetrachloride in chloroform. Aluminium chloride did not react in the cold with the 2-toluene-*p*-sulphonate or 2-trichloroacetate of β-D-glycopyranose 1 : 3 : 4 : 6-tetra-acetate, probably because of the weakening of the nucleophilic properties by the strong inductive effects in the toluene-*p*-sulphonyloxy- and

[4] Lemieux, *Adv. Carbohydrate Chem.*, 1954, **9**, 1.
[5] Pacsu, *ibid.*, 1945, **1**, 77.
[6] Frush and Isbell, *J. Res. Nat. Bur. Stand.*, 1941, **27**, 413.
[7] Haynes and Newth, *Adv. Carbohydrate Chem.*, 1955, **10**, 207.
[8] Pacsu and Rich, *J. Amer. Chem. Soc.*, 1935, **57**, 587.
[9] Montgomery, Hann, and Hudson, *ibid.*, 1937, **59**, 1124.
[10] Lemieux and Brice, *Canad. J. Chem.*, 1952, **30**, 295.

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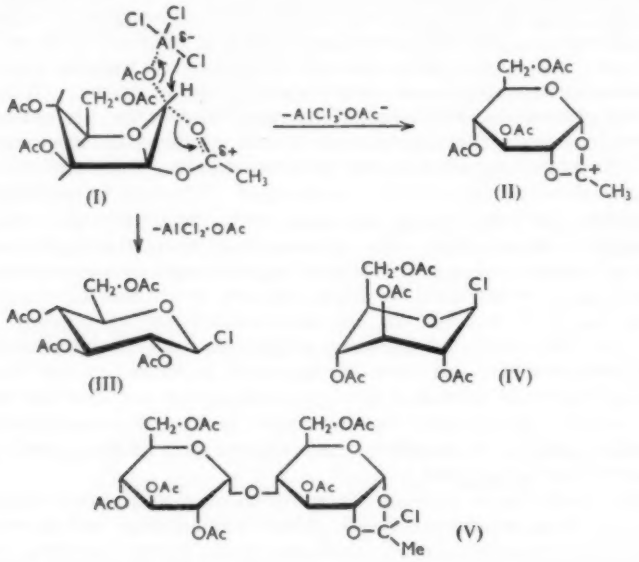
the trichloroacetoxy-group. The 6-toluene-*p*-sulphonyloxy-group in β-D-glucopyranose 1 : 3 : 4 : 6-tetra-acetate 6-toluene-*p*-sulphonate had no detectable effect on the normal displacement at $C_{(1)}$. 2-Acetamido-1 : 3 : 4 : 6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose



did not react with aluminium chloride. The acetamido-group is known to show neighbouring-group reactivity in carbohydrates,[11,12] and the reaction may have failed through the sparing solubility of the compound, or through inactivation of the aluminium chloride by co-ordination to nitrogen.

" β-Acetochloroglucose " and the other pyranosyl chlorides (except that from mannose) obtained by the aluminium chloride procedure are isomers of the well-known " stable " acetylglycosyl chlorides, and proof was needed that they are true epimers of the " stable " chlorides. The epimeric nature of " stable " and " unstable " chlorides has been assumed by most workers, except for the " exceedingly sensitive " acetylmaltosyl chloride of Freudenberg and Ivers,[13] which it is generally conceded is one of the isomers of the cyclic orthoacetyl chloride (V). The regular formation of methyl orthoacetates from the " unstable " chlorides in the Koenigs–Knorr synthesis of methyl glycosides [5] is not conclusive, as they may be formed directly from orthoacetyl chlorides of type (V), or from 1 : 2-*trans*-acylglycosyl chlorides by neighbouring-group participation. Zemplen *et al.* have now suggested [3] that " β-acetochloroglucose " is also a cyclic orthoacetyl chloride, because their preparation of it from β-D-glucopyranose penta-acetate and aluminium chloride in cold chloroform was analogous to Pacsu and Rich's preparation [8] of an oily acetylmaltosyl chloride, which the latter assumed to be essentially the same as Freudenberg and Ivers's chloride (V). This argument was disproved by our finding that the reaction of β-maltose octa-acetate with aluminium chloride in cold chloroform affords a stable, crystalline compound having properties to be expected of the hitherto unknown hepta-*O*-acetyl-β-maltosyl chloride. Like other chlorides obtained by the aluminium chloride procedure, it differed from Freudenberg and Ivers's chloride in being relatively

[11] Baker and Schaub, *J. Amer. Chem. Soc.*, 1953, **75**, 3864.
[12] Jeanloz, *ibid.*, 1957, **79**, 2591; Tarasiejska and Jeanloz, *ibid.*, p. 4215.
[13] Freudenberg and Ivers, *Ber.*, 1922, **55**, 929.

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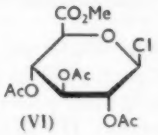
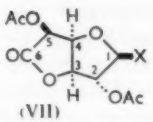
resistant to hydrolysis when dissolved in moist benzene, which rapidly hydrolysed compound (V).[14] Gagolski [1] seems to have prepared the new maltosyl chloride in impure form, and it presumably was the major component of Pacsu and Rich's oily product.[8]



(VI)



(VII)

Optical rotations of the products of the aluminium chloride procedure are consistent with the true acetylglycosyl chloride structures.[15] Further evidence that the compounds are not orthoacetyl chlorides was found in their reaction with silver acetate in benzene. The orthoacetyl maltosyl chloride (V) reacted readily with silver acetate in cold benzene, giving a maltose octa-acetate different from the known α- and β-octa-acetates.[14] The 1 : 2-*trans*-chloride-acetates from the aluminium chloride reaction were relatively unreactive toward silver acetate in cold benzene, but at the b. p. afforded the sugar acetates of 1 : 2-*trans*-configuration from which they had been prepared. Chlorides of 1 : 2-*cis*-configuration also afforded sugar acetates of 1 : 2-*trans*-configuration at the b. p., but far more slowly. The greater reactivity of the 1 : 2-*trans*-chloride-acetates is due to participation of the 2-acyl group in the displacement at position 1, by way of the ion (II). The rate of reaction with silver acetate in benzene permits discrimination between the three classes of poly-*O*-acetylglycosyl chloride.

The structures and configurations, hitherto doubtful, of some chlorides related to D-glucuronic acid have been clarified by their preparation by the aluminium chloride method. Methyl tetra-*O*-acetyl-β-D-glucopyranuronate of known structure and configuration (see p. 644) afforded, on reaction with aluminium chloride, a chloride with m. p. 150—151° and $[\alpha]_D$ −17° (rotations in chloroform), identical with a compound obtained by Goebel and Babers by treating an acetylated methyl D-glucuronate of unproven structure with hydrogen chloride in acetyl chloride.[16c] The compound is, therefore, methyl 2 : 3 : 4-tri-*O*-acetyl-1-chloro-1-deoxy-β-D-glucopyranuronate (VI); the configuration is confirmed by the optical rotation [15] and by the reconversion of the chloride into the parent tetra-acetate by silver acetate in boiling benzene. Three different incorrect structures have been suggested for this chloride.[16d, 4, 7] Goebel and Babers obtained an isomeric compound with m. p. 99—100° and $[\alpha]_D$ +169°, which is now seen to be the α-anomer of (VI), by refluxing the acetate used for making (VI) with titanium tetrachloride in chloroform.[16d]

The same authors [16b] prepared an acetylglycosyl chloride with m. p. 108—109° and $[\alpha]_D$ +96° by treating acetylated D-glucurone with hydrogen chloride in acetyl chloride. The furanoid structure of D-glucurone [17] and its triacetates [18] seems to be well established, and as the β-triacetate [16a, 18] readily reacted with aluminium chloride in cold chloroform, affording a chloride identical with that described by Goebel and Babers,[16b] their product is probably 2 : 5-di-*O*-acetyl-1-chloro-1-deoxy-β-D-glucofuranurono-6 ⟶ 3-lactone (VII; X = Cl). Chemical evidence consistent with this configuration is found in the formation of a methyl orthoacetate under Koenigs–Knorr conditions,[19] and in the ready regeneration of the β-triacetate (VII; X = OAc) from the chloride by silver acetate in acetic acid. This evidence does not completely exclude an orthoacetyl chloride structure, as the 5-acetoxy-group in the lactone (VII) is close enough to participate in displacements at position 1. Consideration of the optical rotations of the chloride and of the α- and the

[14] Freudenberg, von Hochstetter, and Engels, *Ber.*, 1925, **58**, 666.
[15] Korytnyk, following paper.
[16] Goebel and Babers, *J. Biol. Chem.*, (*a*) 1933, **100**, 743; (*b*) 1933, **101**, 173; (*c*) 1934, **106**, 63; (*d*) 1935, **111**, 347.
[17] Smith, *J.*, 1944, 584.
[18] Tsou and Seligman, *J. Amer. Chem. Soc.*, 1952, **74**, 5605.
[19] Goebel and Babers, *J. Biol. Chem.*, 1935, **110**, 707.

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β-triacetate of D-glucurone (+204° and +84°, respectively)[16a] strongly favours the β-configuration for the chloride. If this is correct, it is surprising that reaction with silver acetate or aluminium chloride should occur readily at an *endo*-position in the bicyclic system (VII). Bulky reagents do not attack at *endo*-positions in the related ring system of the 1 : 4-3 : 6-dianhydrohexitols.[20]

β-D-Fructopyranose penta-acetate reacted only slowly with aluminium chloride in chloroform, and refluxing was needed to give a good yield of tetra-*O*-acetyl-β-D-fructopyranosyl chloride, which is also obtained by using more powerful reagents. There was no evidence of the formation of an isomeric chloride. The sluggish reaction is probably due to hindrance to the attachment of aluminium chloride to the 2-acetoxy-group, as the 1-acetoxy-group is favourably placed to participate in the displacement step.

Reducing sugars with a free hydroxyl group at the hemiacetal carbon also give chlorides when treated with aluminium chloride if a neighbouring acyl group is correctly orientated to assist in displacement of the hydroxy-group. β-D-Galactopyranose 2 : 3 : 4 : 6-tetra-acetate reacted in the usual way, affording tetra-*O*-acetyl-β-D-galactopyranosyl chloride, but the α-D-tetra-acetate did not react under these conditions. β-D-Fructopyranose 1 : 3 : 4 : 5-tetra-acetate afforded a fair yield of tetra-*O*-acetyl-β-D-fructopyranosyl chloride in the cold; it is therefore more reactive than the fructose penta-acetate.

The 1 : 2-*trans*-glycosyl chlorides are practically unaffected by short contact with aluminium chloride in chloroform at room temperature, but at higher temperatures epimerisation to the more stable 1 : 2-*cis*-chloride-acetates may occur. Tetra-*O*-acetyl-β-D-glucopyranosyl chloride readily afforded the α-chloride when refluxed with aluminium chloride in chloroform. Tetra-*O*-acetyl-β-D-galactopyranosyl chloride was also transformed under these conditions, but the product had a specific rotation (+177·5°) lower than the accepted value[21] for the α-isomer (+212·3°). Repetition of Skraup and Kremann's preparation of the α-galactosyl chloride showed that their reported rotation is wrong, and the β-chloride is in fact completely transformed into α-chloride by aluminium chloride. 2 : 3 : 4-Tri-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranosyl chloride and methyl 2 : 3 : 4-tri-*O*-acetyl-1-chloro-1-deoxy-β-D-glucopyranuronate resisted epimerisation by aluminium chloride, and their stability may be due to the larger, more electronegative groups at position 6.

Anhydrous aluminium bromide was allowed to react with β-D-glucopyranose penta-acetate in cold chloroform in the hope that tetra-*O*-acetyl-β-D-glucopyranosyl bromide would be formed, but the only crystalline product isolated was tetra-*O*-acetyl-β-D-glucopyranosyl *chloride*. Since this was formed under conditions identical with those used for reaction of the glucose penta-acetate with aluminium chloride, an extremely rapid exchange of halogen must occur between aluminium bromide and chloroform. There may be a risk of halogen exchange in the preparation of poly-*O*-acetylglycosyl bromides by refluxing acetylated sugars with titanium tetrabromide in chloroform.[22]

All 1 : 2-*trans*-*O*-acetylglycosyl chlorides except methyl 2 : 3 : 4-tri-*O*-acetyl-1-chloro-1-deoxy-β-D-glucopyranuronate showed a slow rotational change when dissolved in nominally "dry" chloroform, and larger, more rapid changes in ordinary chloroform. A detailed study of the behaviour of tetra-*O*-acetyl-β-D-glucopyranosyl chloride in chloroform of varying moisture content showed that the change was negligible in very rigorously dried chloroform, but successive increases in the ratio of water to β-chloride in the solutions caused more extensive and more prolonged changes in rotation. No crystalline material could be isolated from the chloroform solutions after the changes had ceased, and the oils recovered contained ionic chlorine. Contrary to the common belief[4,7] the changes are not true mutarotations indicative of simple anomerisation to the more stable α-chloride, but are due to hydrolysis; and the change of rotation to more positive values, and the

[20] Matheson and Angyal, *J.*, 1952, 1133; Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[21] Skraup and Kremann, *Monatsh.*, 1901, **22**, 375.
[22] Zemplen and Gerecs, *Ber.*, 1934, **67**, 2049.

known course of the hydrolysis of the β-chloride in moist acetic acid,[23] suggest that the primary product is α-D-glucopyranose 2 : 3 : 4 : 6-tetra-acetate. The early observation [24] that the rate of change of rotation of "β-acetochloroglucose" in various solvents increased with the dielectric constant of the solvent is as consistent with hydrolysis by traces of moisture as with the simple anomerisation originally postulated, the rate of each reaction being determined by solvation and ionisation of the chlorine. The "mutarotation" of an acyclic acetylglycosyl chloride in "dry" chloroform was found to be accompanied by hydrolysis. [25] It is likely that all chlorides of 1 : 2-*trans*-configuration would be stable in perfectly dry, non-polar solvents.

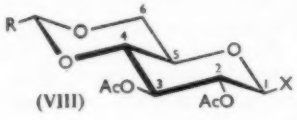
Conditions favourable for rapid hydrolysis of acylglycopyranosyl chlorides by traces of water should be an equatorial orientation (usually β) of the chlorine atom, a solvent with good solvating power for chloride ions, and a neighbouring acyl group capable of participating in the solvolytic displacement of chlorine. Available data for acylated aldohexopyranosyl halides or the related aldoheptopyranosyl halides [4] show that the halide containing equatorial halogen is the thermodynamically less stable of a pair of epimers, and because of its lower stability and the greater accessibility of the halogen atom to solvation the equatorial halide should be more readily hydrolysed, other factors being equal. Participation by the neighbouring acyl group is, however, the most important single factor promoting rapid hydrolysis, because the cyclic ion (II) is highly reactive and, once formed, acts as a scavenger for traces of water.[26] When neighbouring-group participation is ineffective, true epimerisation of halogen without hydrolysis is possible, as with 3 : 4 : 6-tri-*O*-acetyl-β-D-glucopyranosyl chloride, which mutarotates in acetone, affording a solution from which the α-anomer may be isolated.[27] Water is required in this reaction, probably to assist the ionisation of the β-chloride by solvation, because it was found that the β-chloride could be recovered unchanged after four days in scrupulously dried, pure acetone, whereas the same solvent briefly exposed to moist air converted it into the α-chloride. Brigl's speculation on the rôle of water in the mutarotation of this β-chloride [28] is thereby confirmed. The stability of the glucuronosyl chloride (VI) in chloroform (it is also unaffected by aluminium chloride in refluxing chloroform) shows that other factors, probably electronic, may sometimes override the more obvious steric factors.

Lemieux and his colleagues have postulated that a conformational change is required in some pyranose sugars if neighbouring groups are to participate in displacement reactions.[4, 26, 29] For example, tetra-*O*-acetyl-β-D-glucopyranosyl chloride changes from the stable C1 conformation (III) to the alternative 1C chair conformation (IV) to provide the favourable antiparallel arrangement of the chlorine atom and the 2-acetoxy-group. They further postulate that the cyclic ion (II) formed by the displacement at $C_{(1)}$ has a half-chair conformation analogous to that of *cyclo*hexene, and have correlated differences in reactivity of several pyranose sugar acetates of 1 : 2-*trans*-configuration with the arrangement of substituents in the two possible half-chair conformations of the carbonium ions.[30] Our experience with derivatives of 4 : 6-*O*-benzylidene- and 4 : 6-*O*-ethylidene-D-glucose shows that part of this thesis must be modified.

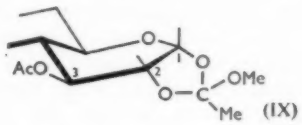
4 : 6-*O*-Benzylidene-β-D-glucopyranose triacetate (VIII; R = Ph, X = OAc) reacted smoothly with aluminium chloride in cold chloroform, affording the corresponding β-chloride (VIII; R = Ph, X = Cl) as a stable, crystalline compound. When refluxed with silver acetate in benzene, this regenerated the β-triacetate. With methanol, in the presence of silver carbonate, quinoline, or collidine, it gave a crystalline compound

[23] Lemieux and Brice, *Canad. J. Chem.*, 1955, **33**, 109.
[24] Schlubach, Stadler, and Wolf, *Ber.*, 1928, **61**, 287.
[25] Wolfrom, Konigsberg, and Moody, *J. Amer. Chem. Soc.*, 1940, **62**, 2343.
[26] Lemieux and Cipera, *Canad. J. Chem.*, 1956, **34**, 906.
[27] Lemieux and Huber, *ibid.*, 1953, **31**, 1040.
[28] Brigl, *Z. physiol. Chem.*, 1921, **116**, 1.
[29] Lemieux, Brice, and Huber, *Canad. J. Chem.*, 1955, **33**, 134.
[30] Lemieux and Brice, *ibid.*, 1956, **34**, 1006.

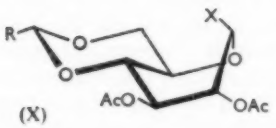
formulated as the 1 : 2-(methyl orthoacetate) (partial structure IX). Hydrolysis of the methyl orthoacetate with ammonia, followed by methylation (Purdie) and vigorous acidic hydrolysis, afforded 3-*O*-methyl-D-glucose, showing that an alkali-labile group was present at position 3, and alkali-stable, acid-labile substituents at the other positions. Treatment of the methyl orthoacetate with anhydrous acetic acid regenerated the 4 : 6-*O*-benzylidene β-triacetate (VIII; R = Ph, X = OAc) [cf. the analogous behaviour of α-D-glucopyranose 3 : 4 : 6-triacetate 1 : 2-(ethyl orthoacetate) [26]]. A solution of the methyl orthoacetate in 99% acetic acid [26] showed a very rapid increase in optical rotation, followed by a decrease. The product isolated from this solution at the point of maximum rotation seemed to be 4 : 6-*O*-benzylidene-α-D-glucopyranose 2 : 3-diacetate; it was also



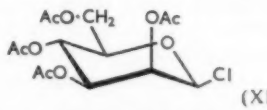
(VIII)



(IX)



(X)



(XI)

obtained by treating the β-chloride (VIII; R = Ph, X = Cl) with silver carbonate and silver nitrate in aqueous acetone. The methoxy-group is therefore more labile to acid than the benzylidene group. This proves that the product was the authentic 1 : 2-(methyl orthoacetate) (IX), and it is virtually certain that the chloride from which it was made is the true glycopyranosyl chloride of β-D-configuration, and that the reaction of aluminium chloride with the β-triacetate has followed the normal course, without affecting the cyclic acetal grouping. The action of aluminium chloride on 4 : 6-*O*-ethylidene-β-D-glucopyranose triacetate (VIII; R = Me, X = OAc) afforded a chloride similar in all respects to the 4 : 6-*O*-benzylidene chloride, and it is therefore (VIII; R = Me, X = Cl).

The rates of formation of these chlorides from the bicyclic systems (VIII), and of the subsequent reactions of the chlorides, were qualitatively similar to rates for the monocyclic pyranose compounds previously studied, even though the *trans*-junction of the rings in (VIII) prevents the pyranose ring from passing into the 1C conformation. Structure (VIII) may, however, pass without undue conformational strain into the boat-form (X), which has the required antiparallel arrangement about positions 1 and 2. Transformation of monocyclic derivatives of β-D-glucopyranose into an analogous boat form during reaction is probable, as the 1C chair form (IV) involves excessive steric strains. Our experiments do not disprove the half-chair conformation for the carbonium ion formed by participation of the 2-acetoxy-group in displacements at position 1, but only one half-chair form is possible from the structure (VIII).

Both epimers of acetylated aldopyranosyl chlorides are now readily available in all cases where the 1 : 2-*trans*-chloride-acetate, obtainable by the aluminium chloride method, contains an equatorial chlorine atom and is therefore the less stable isomer, provided the acetylated sugar is stable enough to permit the use of the more powerful reagents, such as titanium tetrachloride, required for formation of the more stable 1 : 2-*cis*-chloride-acetate (axial). If the pure 1 : 2-*trans*-sugar acetate needed for the aluminium chloride method is not known, it can be made by the action of silver acetate on the chloride or bromide of 1 : 2-*cis*-configuration, which can usually be prepared from a crude mixture of the epimeric acetates. If the 1 : 2-*trans*-compound contains axial chlorine (aldoses of *manno-*, *talo-*, *altro-*, or *ido*-configuration), it will be the stable epimer, and be formed by the action of either aluminium chloride or titanium tetrachloride; in such cases, no general route to the 1 : 2-*cis*-chloride-acetate is available.

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Hydrogen chloride in acetyl chloride, used by Goebel and Babers [16b, 16c] in preparing the glucuronosyl chlorides (VI) and (VII), is a neglected reagent. In the two examples cited, it gave the same isomer as was obtained by the aluminium chloride method. Experiments with various sugar acetates, exposed to the action of hydrogen chloride in acetyl chloride under standardised conditions, showed that this apparent similarity between the two reactions is not general. Both the α- and the β-penta-acetate of methyl D-glucopyranuronate afforded about 70% of the β-chloride (VI). Somewhat lower yields (54—62%) of tetra-*O*-acetyl-β-D-glucopyranosyl chloride were obtained from both the α- and the β-penta-acetate of D-glucopyranose; optical rotations of the crude reaction mixture suggested that about 30% of α-chloride was also present. From reactions of the β-octa-acetates of maltose and lactose only the α-chlorides could be isolated, in 65% yield. β-D-Fructopyranose 1 : 3 : 4 : 6-tetra-acetate gave about 76% of tetra-*O*-acetyl-β-D-fructopyranosyl chloride.

β-D-Mannopyranose penta-acetate afforded two products under the the same conditions, tetra-*O*-acetyl-α-D-mannopyranosyl chloride (63% isolated) and a new compound, tetra-*O*-acetyl-β-D-mannopyranosyl chloride (XI) (1% isolated); polarimetry showed that the ratio of α- to β-chloride in the crude mixture was about 83 : 17. α-D-Mannopyranose penta-acetate afforded 76% of crude α-chloride, and no β-chloride (XI) could be isolated. The new chloride (XI) is the first example of an acetylated aldopyranosyl chloride of 1 : 2-*cis*-configuration that definitely contains an equatorial chlorine atom. Lack of material has prevented an exhaustive study of it, but it shows the stability expected of 1 : 2-*cis*-acylglycosyl chlorides. It was recovered unchanged after two months from a solution in chloroform, and reacted slowly with silver acetate in boiling benzene, affording α-D-mannopyranose penta-acetate. Hydrogen chloride in acetyl chloride caused partial epimerisation to the α-chloride. The new chloride has a higher melting point than the α-chloride; the same relation was noted for every other α, β pair of acetylated aldopyranosyl chlorides examined.

The action of hydrogen chloride in acetyl chloride on sugar acetates deserves further study, especially of the course of the reaction with time. The diverse stereochemical results of the reaction when applied under fixed conditions to the acetates listed above may merely be due to different rates of epimerisation of starting material and product for the various sugars. The successful isolation of the new 1 : 2-*cis*-chloride-acetate (XI) from mannose, even though in poor yield, suggests that the reaction should be tried with sugar acetates of *talo-*, *altro-*, and *ido*-configuration. If a mixture of chlorides is obtained, it is possible that enrichment in 1 : 2-*cis*-compound might be achieved by selective destruction of the more reactive 1 : 2-*trans*-isomer, either hydrolytically or by other means.

Experimental

Optical rotations were measured in ordinary chloroform, unless otherwise stated.

Materials.—Anhydrous aluminium chloride was resublimed, and crushed with exclusion of moisture, just before use. Chloroform used for the syntheses was freed from alcohol and distilled over phosphoric oxide. Acetylated sugars were recrystallised from ether and dried in a high vacuum. The majority were known compounds, made by standard methods.

1 : 3 : 4 : 6-*Tetra*-O-*acetyl*-2-O-*benzoyl*-β-D-*glucopyranose* was prepared by benzoylation of β-D-glucopyranose 1 : 3 : 4 : 6-tetra-acetate [27] in pyridine at 0°. It was crystallised twice from alcohol and twice from ether, and obtained as fine needles, m. p. 184—184·5°, $[\alpha]_D$ +45·0° (*c* 0·7) (Found: C, 56·2; H, 5·5. $C_{21}H_{24}O_{11}$ requires C, 55·8; H, 5·3%). 1 : 3 : 4 : 6-*Tetra*-O-*acetyl*-2-O-*toluene*-p-*sulphonyl*-β-D-*glucopyranose* was similarly prepared and obtained as needles (from methanol), m. p. 157—158°, $[\alpha]_D^{23}$ +22·3° (*c* 0·7) (Found: S, 6·5. $C_{21}H_{26}O_{12}S$ requires S, 6·4%).

The original directions for the preparation of methyl tetra-*O*-acetyl-β-D-glucopyranuronate [16c] do not adequately define the ring size or configuration. β-D-Glucopyranose 1 : 2 : 3 : 4-tetra-acetate was oxidised with potassium permanganate,[31] and the oily product

[31] Stacey, *J.*, 1939, 1529.

was esterified with diazomethane. Several recrystallisations of the impure methyl ester from alcohol gave material with m. p. 176—177°, $[\alpha]_D^{22}$ +5·9° (*c* 0·8), which proved to be identical with that obtained according to Goebel and Babers [16c] by methanolysis of D-glucofuranurono-6 ⟶ 3-lactone and acetylation of the oily product (Found: C, 48·2; H, 5·4. Calc. for $C_{15}H_{20}O_{11}$: C, 47·9; H, 5·4%). The permanganate oxidation of β-D-glucopyranose 1 : 2 : 3 : 4-tetra-acetate gave variable yields, and attempts were made to use chromium trioxide in glacial acetic acid, and also liquid nitrogen dioxide, as oxidants, but pure material could not be isolated from the products of such oxidations.

4 : 6-*O*-Benzylidene-β-D-glucopyranose triacetate [32] was prepared by the acetylation of somewhat impure 4 : 6-*O*-benzylidene-D-glucose with acetic anhydride and sodium acetate at 100°. The crude material was recrystallised from ether and obtained as plates, m. p. 198—199°, $[\alpha]_D^{17}$ −52·1° (*c* 0·9); Zervas [32] reported similar constants. Like Zervas, we obtained a small yield of a by-product, which had m. p. 154°, $[\alpha]_D^{17}$ +48·6° (*c* 1), after several recrystallisations from alcohol and ether. This may have been the corresponding α-triacetate contaminated with a compound containing less carbon (Found: C, 56·3; H, 5·5. Calc. for $C_{19}H_{22}O_9$: C, 57·8; H, 5·6%). Lengthy fractional crystallisation did not afford a demonstrably pure compound.

4 : 6-O-*Ethylidene*-β-D-*glucopyranose triacetate* was prepared in a similar way from 4 : 6-*O*-ethylidene-D-glucose.[33] The crude product crystallised when the reaction mixture was diluted with ice and water, and one recrystallisation from methanol afforded material with m. p. 117—119° in 67% yield. Two crystallisations from ether–light petroleum gave the pure compound as needles, m. p. 122—123°, $[\alpha]_D^{23}$ −28·8° (*c* 1) (Found: C, 51·0; H, 6·1. $C_{14}H_{20}O_9$ requires C, 50·6; H, 6·1%). Acetylation of 4 : 6-*O*-ethylidene-D-glucose with acetic anhydride and pyridine at room temperature gave only syrups.

Reactions with Aluminium Chloride.—(a) *Fully acetylated sugars.* β-D-Galactopyranose penta-acetate (5 g.) was dissolved in pure, dry chloroform (25 ml.), crushed aluminium chloride (0·9 g., 0·53 mole) was added, and the mixture was shaken at room temperature for 30 min. Aluminium chloride gradually disappeared and was replaced by a fine white precipitate. The mixture was then filtered directly into a large volume (750 ml.) of dry hexane (cf. Gagolski [1]), and the resulting precipitate was also filtered off. Evaporation of the hexane and chloroform under reduced pressure afforded crystals, from which last traces of solvent were removed in a high vacuum. The crude tetra-*O*-acetyl-β-D-galactopyranosyl chloride was dissolved in ether, and light petroleum (b. p. below 40°) was added to turbidity, the practically pure β-chloride then crystallising in 80% yield. After one more crystallisation it had m. p. 93°, $[\alpha]_D^{20}$ +14·9° (*c* 0·9), and was identical with the compound obtained by Schlubach and Gilbert's method.[34] Use of a large excess of aluminium chloride reduced the yield, whereas a shortened period of reaction, or reduction of aluminium chloride to the theoretical amount, gave a product contaminated with D-galactose penta-acetate.

β-D-Galactofuranose penta-acetate [35] afforded an 88% yield of tetra-*O*-acetyl-β-D-galactofuranosyl chloride [35, 36] under the above conditions. The purified product had m. p. 72—73° (somewhat higher than previously reported [36]) and $[\alpha]_D^{23}$ −78·7° (*c* 1).

Tri-*O*-acetyl-β-D-xylopyranosyl chloride [34] was prepared from β-D-xylopyranose tetra-acetate by a more convenient method. The proportion of reagents was the same as in the first example, but shaking was continued for 40 min., and the mixture was then diluted with pure benzene, salts were removed by three extractions with ice-water, and the benzene solution was dried ($CaCl_2$). Solvents were evaporated below 45°, and the crude β-chloride was recrystallised twice from ether–light petroleum. It then had m. p. 112—113°, $[\alpha]_D^{23}$ −141·0° (*c* 1) (yield 90%).

The last procedure was also used to obtain the following chlorides from the appropriate acetylated sugars (β-D-configurations): 2 : 3 : 4-*tri*-O-*acetyl*-6-O-*toluene*-p-*sulphonyl*-β-D-*glucopyranosyl chloride* (40% yield), m. p. 160—161° (from ether), $[\alpha]_D^{22}$ +9·0° (initial) ⟶ +32° (19 hr.) (*c* 0·7) (Found: C, 47·9; H, 4·8; S, 6·7; Cl, 7·3. $C_{19}H_{23}O_{10}SCl$ requires C, 47·7; H, 4·8; S, 6·7; Cl, 7·4%); *methyl* 2 : 3 : 4-*tri*-O-*acetyl*-1-*chloro*-1-*deoxy*-β-D-*glucopyranuronate*

[32] Zervas, *Ber.*, 1931, **64**, 2289.
[33] Hockett, Collins, and Scattergood, *J. Amer. Chem. Soc.*, 1951, **73**, 599.
[34] Schlubach and Gilbert, *Ber.*, 1930, **63**, 2292.
[35] Schlubach and Prochownick, *ibid.*, p. 2298.
[36] Hudson and Johnson, *J. Amer. Chem. Soc.*, 1916, **38**, 1223.

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(67% yield), m. p. 149—150°, $[\alpha]_D^{18}$ −16·9° (no change in 24 hr.) (*c* 0·5) (Found: C, 44·5; H, 4·9; Cl, 10·7. $C_{13}H_{17}O_9Cl$ requires C, 44·1; H, 4·9; Cl, 10·0%); and 3 : 4 : 6-*tri*-O-*acetyl*-2-O-*benzoyl*-β-D-*glucopyranosyl chloride* (80% yield), m. p. 124—125° (Found: Cl, 8·0. $C_{19}H_{21}O_9Cl$ requires Cl, 8·3%).

β-D-Fructopyranose penta-acetate gave only traces of organic chloro-compound after 90 minutes' shaking in the cold, and reaction was incomplete after 15 min. at the b. p. After 30 min. at the b. p., a nearly quantitative yield of tetra-*O*-acetyl-β-D-fructopyranosyl chloride was obtained, with m. p. 82—83°, not depressed on admixture with an authentic sample.[37]

(b) *Acetylated sugars with the hemiacetal hydroxyl group free.* When β-D-galactopyranose 2 : 3 : 4 : 6-tetra-acetate [38] was shaken with aluminium chloride in cold chloroform and the mixture was worked up by the above method, tetra-*O*-acetyl-β-D-galactopyranosyl chloride, identical with the product obtained from the penta-acetate, was recovered in 50% yield. β-D-Fructopyranose 1 : 3 : 4 : 5-tetra-acetate [39] was largely converted into tetra-*O*-acetyl-β-D-fructopyranosyl chloride within 80 min. at room temperature, a small part of starting material being unchanged.

(c) *Compounds not reacting significantly.* Treatment of α-D-galactopyranose penta-acetate, α-D-galactofuranose penta-acetate,[36] α-D-galactopyranose 2 : 3 : 4 : 6-tetra-acetate,[36] and 2-acetamido-1 : 3 : 4 : 6-tetra-*O*-acetyl-2-deoxy-β-D-glucopyranose [40] with aluminium chloride in cold chloroform did not afford detectable quantities of chloro-compounds.

The reagents had no effect at the b. p. on 1 : 3 : 4 : 6-tetra-*O*-acetyl-2-*O*-trichloroacetyl- or 1 : 3 : 4 : 6-tetra-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-β-D-glucopyranose, and the latter was also unaffected by titanium tetrachloride in refluxing chloroform. In attempts to force reaction, the acetates were refluxed with pure titanium tetrachloride (10 ml. for 0·4 g. of acetate) for 2—3 min., then the solutions were quickly cooled and stirred into ice-water. The former acetate yielded only an unidentified oil, but the latter gave about 5% of 3 : 4 : 6-tri-*O*-acetyl-2-*O*-toluene-*p*-sulphonyl-α-D-glucopyranosyl chloride, obtained as plates (from ether–light petroleum), m. p. 120—122° (not depressed on admixture with authentic material [41]), $[\alpha]_D^{21}$ +134·5° (*c* 0·8).

β-D-Glucopyranose pentabenzoate was prepared by the method of Ness, Fletcher, and Hudson,[42] but its m. p. could not be raised above 161—165°; it had $[\alpha]_D^{16}$ +22·6° (*c* 1·2). It did not react with aluminium chloride. When it was dissolved in a solution of titanium tetrachloride (2·5% v/v) in chloroform, and the mixture was set aside for 30 min. before being worked up by the methods used in experiments with aluminium chloride, a solid of indefinite m. p. was obtained, having $[\alpha]_D^{16}$ +14·2° and containing only 1% of chlorine.

Epimerisations by Aluminium Chloride.—A solution of tetra-*O*-acetyl-β-D-galactopyranosyl chloride (2·5 g.) in pure chloroform (20 ml.) was refluxed for about 15 min. with anhydrous aluminium chloride (0·45 g., 0·5 mol.), then the product was isolated in the usual way, being obtained as fine needles, m. p. 78—79°, $[\alpha]_D^{25}$ +175·1° (*c* 1), in 88% yield. Many crystallisations from light petroleum did not change the m. p., and the rotation changed only to $[\alpha]_D^{25}$ +177·5° (*c* 1). Tetra-*O*-acetyl-α-D-galactopyranosyl chloride, prepared by Skraup and Kremann's method,[21] had identical properties.

Tetra-*O*-acetyl-β-D-galactofuranosyl chloride and tri-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranosyl chloride did not afford identifiable products when refluxed for 30 and 40 min., respectively, under conditions similar to the above. Methyl tri-*O*-acetyl-1-chloro-1-deoxy-β-D-glucopyranuronate was recovered after being refluxed for 40 min.

Reactions of 1 : 2-trans-*Chloride-acetates with Silver Acetate.*—When a solution of tetra-*O*-acetyl-β-D-glucopyranosyl chloride (0·4 g.) in dry benzene (6 ml.) was refluxed with finely divided silver acetate (0·2 g.), chlorine was still detectable in the solution after 45 min. After 2 hr., the reaction was apparently complete, whereupon the solution was filtered and the benzene was evaporated, leaving an oil that crystallised on addition of ether. The product was β-D-glucopyranose penta-acetate. Tetra-*O*-acetyl-α-D-glucopyranosyl chloride was treated in the same way, but organic chloride was still present after 24 hr. After 48 hr., a high yield of pure β-D-glucopyranose penta-acetate was obtained.

[37] Brauns, *J. Amer. Chem. Soc.*, 1920, **42**, 1846.
[38] Compton and Wolfrom, *ibid.*, 1934, **56**, 1157.
[39] Pacsu and Rich, *ibid.*, 1933, **55**, 3018.
[40] Bergmann and Zervas, *Ber.*, 1931, **64**, 975.
[41] Reynolds, *J.*, 1931, 2626.
[42] Ness, Fletcher, and Hudson, *J. Amer. Chem. Soc.*, 1950, **72**, 2200.

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A solution of 2 : 3 : 4-tri-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranosyl chloride (0·1 g.) in anhydrous acetic acid (1 ml.) was shaken overnight with excess of silver acetate. Filtration and evaporation of the solvent under reduced pressure afforded tetra-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl-β-D-glucopyranose (70%).

Methyl 2 : 3 : 4-tri-*O*-acetyl-1-chloro-1-deoxy-β-D-glucopyranuronate, dissolved in benzene, was unchanged after 3 hours' shaking with a large excess of silver acetate. When the mixture was refluxed for 3 hr., methyl tetra-*O*-acetyl-β-D-glucopyranuronate of high purity was obtained.

Hepta-O-acetyl-β-maltosyl Chloride.—β-Maltose octa-acetate (5 g.), dissolved in chloroform (5 ml.), was shaken with finely divided aluminium chloride (1·2 g.) for 3·5 hr. Solids were crushed under the solution, and shaking was continued for 45 min. The mixture was worked up by the method used for the xylosyl chloride, and the crude product was crystallised once from ether, affording an 81% yield of material with m. p. 123—124°, $[\alpha]_D^{18}$ +54·4° (*c* 0·7). Three further crystallisations afforded pure *hepta-O-acetyl-β-maltosyl chloride*, m. p. 125°, $[\alpha]_D^{18}$ +57·4° (*c* 0·9) (Found: C, 47·6, 47·8; H, 5·4, 5·4; Cl, 4·9, 5·9; $CH_3{\cdot}CO$, 47·2. $C_{26}H_{35}O_{17}Cl$ requires C, 47·7; H, 5·4; Cl, 5·4; $7CH_3{\cdot}CO$, 46·0%). The pure chloride could be stored for long periods in a desiccator. The preparation was reproducible.

The β-maltosyl chloride was unchanged 3 hr. after being dissolved in benzene that had been emulsified with water. β-Maltose octa-acetate was obtained in 68% yield when the chloride (0·2 g.) in benzene (2 ml.) was refluxed with silver acetate (0·1 g.) for 48 hr. Much organic chloride was present after 2 hr., and some after 12 hr., but β-maltose octa-acetate was isolated after 12 hr.

β-Maltosyl chloride (0·5 g.) was added to a mixture of anhydrous methanol (3 ml.) and collidine (0·5 ml.), and the solution was set aside for 16 hr. Fine needles separated. The mixture was cooled in the refrigerator for 2 hr., then the solid (0·44 g.) was collected and washed with light petroleum. It had m. p. 156—160°, rising to 161—162° after several recrystallisations from methanol; $[\alpha]_D^{19}$ was then +93·2° (*c* 0·7) [Found: C, 50·3; H, 6·1; $CH_3{\cdot}CO$ (by acidic hydrolysis), 46·1. Calc. for $C_{27}H_{38}O_{18}$: C, 49·8; H, 5·9; $7CH_3{\cdot}CO$, 46·3%]. The constants are similar to those reported by Freudenberg, von Hochstetter, and Engels,[14] and by Pacsu and Rich,[8] and the compound is almost certainly hexa-*O*-acetyl-1 : 2-*O*-(1-methoxyethylidene)-α-maltose.

Derivatives of D-Glucofuranurono-6 ⟶ 3-lactone.—1 : 2 : 5-Tri-*O*-acetyl-β-D-glucofuranurono-6 ⟶ 3-lactone was obtained in 87% yield when Tsou and Seligman's procedure [15] was modified by using boron trifluoride in acetic acid (40% w/w) in place of boron trifluoride in ether. A solution of the β-triacetate (1·5 g.) in chloroform (5 ml.) was shaken with aluminium chloride (0·33 g.), and the product was isolated in the usual way. It was recrystallised from ether, and afforded (85% yield) a compound with m. p. 107° and $[\alpha]_D^{21}$ +100° (initial) ⟶ +109° (5 days) (*c* 1), which is considered to be 2 : 5-di-*O*-acetyl-1-chloro-1-deoxy-β-D-glucofuranurono-6 ⟶ 3-lactone. Goebel and Babers [16b] reported m. p. 107·5—108·5°, $[\alpha]_D^{20}$ +95·5° (in $CHCl_3$), for material made by a different method. When a solution of the chloride in anhydrous acetic acid was shaken with silver acetate for 12 hr., the β-triacetate, m. p. 192—193°, was re-formed in 84% yield.

2 : 3-*Di*-O-*acetyl*-4 : 6-O-*benzylidene*-β-D-*glucopyranosyl Chloride.*—A solution of 4 : 6-*O*-benzylidene-β-D-glucopyranose triacetate (2·06 g.) in chloroform (7 ml.) was shaken with aluminium chloride (0·35 g.) for 40 min. The mixture was filtered into benzene (100 ml.), and a solid product was isolated in the usual way. The odour of benzaldehyde was noticeable. One recrystallisation from ether afforded a 72% yield of material with m. p. 175—179°, and several further crystallisations gave the pure O-*benzylidene chloride* as large, hexagonal plates, m. p. 178—179°, $[\alpha]_D^{24}$ −89·2° (initial) ⟶ −45·7° (9 days) (*c* 1·4) (Found: C, 55·0; H, 5·1; Cl, 9·6. $C_{17}H_{19}O_7Cl$ requires C, 55·1; H, 5·1; Cl, 9·6%). It was unchanged for long periods when stored in a desiccator.

4 : 6-*O*-Benzylidene-β-D-glucopyranose triacetate was obtained in 69% yield by refluxing a solution of the above chloride in benzene with silver acetate for 2 hr. A solution of the chloride (0·5 g.) in acetone (5 ml.) was treated with silver carbonate (0·5 g.) and powdered silver nitrate (0·1 g.), and the mixture was vigorously shaken for 5 min. Filtration, followed by rapid evaporation of acetone under reduced pressure and two crystallisations of the residue from ether, afforded a 32% yield of 2 : 3-*di*-O-*acetyl*-4 : 6-O-*benzylidene*-α-D-*glucopyranose*, needles, m. p. 185—187°, $[\alpha]_D^{23}$ +96·5° (*c* 0·8) (Found: C, 58·4; H, 5·8. $C_{17}H_{20}O_8$ requires C, 58·0; H, 5·7%).

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3-O-*Acetyl*-4 : 6-O-*benzylidene*-1 : 2-O-(1-*methoxyethylidene*)-α-D-*glucopyranose*.—This was prepared by three different methods. Suspensions (about 10% w/v) of the 4 : 6-*O*-benzylidene chloride in anhydrous methanol were (*a*) shaken with excess of silver carbonate and anhydrous calcium sulphate at room temperature for 26 hr., (*b*) mixed with 0·1 vol. of anhydrous quinoline, then held at 40° for 4 hr. and set aside at room temperature overnight, or (*c*) mixed with 0·25 vol. of freshly distilled collidine and set aside at room temperature. The solution from (*a*) was filtered and placed in the refrigerator for several days, whereupon it deposited fine needles, m. p. 140—142°. An equal quantity of solid with m. p. 133—135° was obtained by concentrating the mother liquor (total yield, 40%). The solution from (*b*) was concentrated under reduced pressure, the residual oil was dissolved in chloroform, and the solution was extracted in turn with ice-cold hydrochloric acid, ice-cold sodium hydrogen carbonate, and water. Removal of the solvent and dissolution of the residual oil in ether–light petroleum afforded needles, m. p. 138—145°, in 27% yield. The reaction mixture from (*c*) deposited solid within 4 hr. After 21 hr., it was diluted with an equal volume of light petroleum and placed in the refrigerator for 2 hr. The product, when collected and washed with light petroleum, had m. p. 145—147°. Further additions of light petroleum afforded a little more, with m. p. 135—140° (total yield, 87%). When crystallised from ether, the product of each experiment afforded the pure *methyl orthoacetate*, m. p. 148—149°, $[\alpha]_D^{20}$ +36·0° (*c* 0·7) [Found: C, 58·8; H, 6·0; MeO, 8·0; CH_3·CO (by acidic hydrolysis), 23·5. $C_{18}H_{22}O_8$ requires C, 59·0; H, 6·1; MeO, 8·5; $2CH_3$·CO, 23·5%].

The orthoester (380 mg.) was dissolved in methanol (15 ml.) that had been saturated with anhydrous ammonia at 0°, and the mixture was set aside for 7 hr. Methanol and ammonia were removed under reduced pressure, and the residual oil was methylated by being refluxed for 3 hr. with methyl iodide (1 ml.), methanol (1 ml.), and silver oxide (1 g.). The oil recovered by filtration and evaporation of the solution under reduced pressure was further methylated for 3 hr. with methyl iodide (2 ml.) and silver oxide (1 g.). The product recovered at this stage crystallised when mixed with a little ether. A warm ethereal extract of the solid, after being filtered from insoluble matter, deposited 4 : 6-O-*benzylidene*-1 : 2-O-(1-*methoxyethylidene*)-3-O-*methyl*-α-D-*glucopyranose* (48%), long needles, m. p. 130—131°, $[\alpha]_D^{18}$ −63·8° (*c* 0·7) (Found: C, 60·1; H, 6·5; MeO, 17·8. $C_{17}H_{22}O_7$ requires C, 60·3; H, 6·6; MeO, 18·3%). The pure methylated orthoester (160 mg.) was suspended in aqueous 2% hydrochloric acid (25 ml.), and the mixture was set aside for one week. The solution was extracted with ether, treated with silver carbonate in the usual way, and then evaporated under reduced pressure, affording a yellow syrup with $[\alpha]_D^{18}$ +53° (*c* 0·4 in water). Only one reducing sugar could be detected in the syrup, and this moved at the same rate as authentic 3-*O*-methyl-D-glucose on paper chromatography in butan-1-ol–ethanol–water (50 : 10 : 40) or butanol–ethanol–ammonia (*d* 0·88)–water (40 : 10 : 1 : 49) and on ionophoresis in 0·05M-borax buffer. Aniline picrate [43] was used to detect the sugars on paper.

Action of Acetic Acid on 3-O-*Acetyl*-4 : 6-O-*benzylidene*-1 : 2-O-(1-*methoxyethylidene*)-α-D-*glucopyranose*.—(*a*) The ester (100 mg.) was dissolved in carefully purified, anhydrous acetic acid (4 ml.) and set aside for 18 hr. Removal of the solvent under reduced pressure afforded a solid with a strong odour of benzaldehyde. A solution of the solid in warm ether deposited crystals (35 mg.), m. p. 200—201°, identified as 4 : 6-*O*-benzylidene-β-D-glucopyranose triacetate.

(*b*) A solution of the ester (95 mg.) in acetic acid (10 ml.) containing 1% of water showed a rapid change in measured rotation from 0·86° (4 min.) to a maximum of 0·93° (18 min.), followed by a slow decline to 0·87° (5 hr.). At the end of 6 hr., the solvent was removed under reduced pressure and the solid obtained crystallised once from chloroform. The product had m. p. 169—170°, and seemed to be essentially a D-glucose diacetate (Found: C, 45·0; H, 6·1. Calc. for $C_{10}H_{16}O_8$: C, 45·5; H, 6·1%). In a separate experiment, a similar mixture was diluted with a ten-fold volume of toluene after 8 min., and the solvents were immediately evaporated in a high vacuum. Recrystallisation of the solid residue from ether afforded needles (59 mg.), m. p. 173—178°. After several recrystallisations, 2 : 3-di-*O*-acetyl-4 : 6-*O*-benzylidene-α-D-glucopyranose was obtained with m. p. 184—186°, identical with the material described above.

Derivatives of 4 : 6-O-*Ethylidene*-D-*glucose*.—A solution of 4 : 6-*O*-ethylidene-β-D-glucopyranose triacetate (2 g.) in chloroform (10 ml.) was shaken with aluminium chloride (0·4 g.)

[43] Frahn and Mills, *Chem. and Ind.*, 1956, 578.

for 45 min. The product was isolated by the method used for tetra-*O*-acetyl-β-D-galactopyranosyl chloride, and was recrystallised from ether–light petroleum. The crude product (76% yield) had m. p. 170—171°, and after two recrystallisations pure **2 : 3-*di*-O-*acetyl*-4 : 6-O-*ethylidene*-β-D-*glucopyranosyl chloride*** was obtained as plates, m. p. 173—174° (decomp.), $[\alpha]_D^{21}$ −70·0° (initial) ⟶ +7·3° (25 hr.) (*c* 1) (Found: C, 46·9; H, 5·7; Cl, 11·7. $C_{12}H_{17}O_7Cl$ requires C, 46·6; H, 5·6; Cl, 11·5%). The method gave a similar yield if shaking was continued for 6 hr. In rigorously dried chloroform, the specific rotation of the chloride changed only from −70° to −58° during 13·5 days, and about 60% was then recovered from the solution.

A solution of the *O*-ethylidene chloride (0·5 g.) in acetic anhydride (5 ml.) was shaken with silver acetate (0·26 g.) for 6 hr., then the solvent was evaporated under reduced pressure, and the residue was twice recrystallised from ether. **4 : 6-*O*-Ethylidene-β-D-glucopyranose triacetate**, m. p. 121—122°, was obtained in 30% yield.

Treatment of the *O*-ethylidene chloride in acetone with silver carbonate and silver nitrate, under conditions used for the *O*-benzylidene chloride, afforded a substance that crystallised from ether as needles, m. p. 135—136°, $[\alpha]_D^{18}$ +114·5° (*c* 0·9). This is assumed to be **2 : 3-di-*O*-acetyl-4 : 6-*O*-ethylidene-α-D-glucopyranose**. A solution of the *O*-ethylidene chloride in apparently dry acetone showed a change in rotation, $[\alpha]_D^{18}$ −55·0° (initial) ⟶ +104·2° (3 days), and at this stage the same substance, m. p. 135°, could be isolated.

Tetra*-O-*acetyl*-β-D-*mannopyranosyl Chloride.—β-D-Mannopyranose penta-acetate (5 g.) was dissolved in freshly distilled acetyl chloride (10 ml.; "AnalaR") contained in a thick-walled long, narrow tube terminating in a standard ground socket. The lower part of the tube was cooled to about −70° and the contents were saturated with dry hydrogen chloride. The tube was quickly closed with a hollow stopper (lubricated with "Apiezon" grease), to which a closed, narrow side-tube had been sealed. The closed tube was removed from the cooling-bath, the tube and stopper were clamped firmly between rubber pads, and the mixture was held at room temperature for 2 days. Pressure was released by heating the side-tube to softening point, and the acetyl chloride was quickly evaporated under reduced pressure. The residual oil was dissolved in benzene, and the solution was extracted successively with ice-water, ice-cold dilute sodium hydrogen carbonate, and ice-water, and dried ($MgSO_4$). Removal of benzene under reduced pressure afforded an oil, $[\alpha]_D^{17}$ +68·7° (*c* 1·5), which partially crystallised. Two kinds of crystal separated from a solution of the oil in ether on dilution with light petroleum, and were separated by selective decantation of the small quantity of lighter form after the mixture was swirled. The main product (3·0 g.) consisted of large crystals with m. p. 78—80°, and after several recrystallisations it afforded tetra-*O*-acetyl-α-D-mannopyranosyl chloride, m. p. 81° and $[\alpha]_D^{20}$ +89·6° (*c* 0·9), constants very close to those reported for this compound by Pacsu.[44] The minor product (70 mg.) was recrystallised several times from ether, and pure ***tetra*-O-*acetyl*-β-D-*mannopyranosyl chloride*** was obtained as small plates, m. p. 165—166°, $[\alpha]_D^{17}$ −34·1° (unchanged in 24 hr.) (*c* 0·8) (Found: Cl, 9·6. $C_{14}H_{19}O_9Cl$ requires Cl, 9·7%). The chloride was recovered from a solution in purified, anhydrous chloroform after 2 months.

The new mannosyl chloride (200 mg.) was treated with hydrogen chloride in acetyl chloride (2 ml.) under the conditions used in its preparation. The material recovered had $[\alpha]_D^{22}$ +3·8° (*c* 0·8), and crystallisation from ether afforded 43% of starting material with m. p. 164—165°, $[\alpha]_D^{22}$ −33·8° (*c* 1).

A solution of the new chloride (113 mg.) in benzene (1·4 ml.) was refluxed with silver acetate (60 mg.). After 4 hr., considerable quantities of starting material could be recovered, but after 48 hr. the solution did not contain chlorine. Removal of the benzene at this stage gave an oil, $[\alpha]_D$ +39·7° (*c* 0·7), which had an infrared spectrum identical with that of the syrupy α-D-mannopyranose penta-acetate described below, but resisted crystallisation. After a long period, crystals were obtained from it, and identified as α-D-mannopyranose penta-acetate by mixed m. p.

Tetra-*O*-acetyl-α-D-mannopyranosyl chloride was refluxed with silver acetate in benzene in a parallel experiment; the test for organic chloro-compounds was weak after 4 hr., and negative after 6 hr. Evaporation of the benzene afforded a syrup that eventually crystallised from water after it had been distilled at 135° (bath)/10^{-4} mm., and then had m. p. 75—76°, $[\alpha]_D^{22}$ +58·6° (*c* 0·9). Levene and Tipson [45] reported m. p. 74°, $[\alpha]_D$ +56·6° (*c* 1·4), for α-D-mannopyranose penta-acetate.

[44] Pacsu, *Ber.*, 1928, **61**, 1508.
[45] Levene and Tipson, *J. Biol. Chem.*, 1931, **90**, 89.

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Action of Hydrogen Chloride on Other Compounds.—The apparatus and procedure described in the preparation of the β-mannosyl chloride were used, and the period of reaction was generally 2 days. Yields are reported for crude products, but in all cases these readily afforded the pure compounds on recrystallisation.

(a) α-D-*Glucopyranose penta-acetate.* Tetra-*O*-acetyl-β-D-glucopyranosyl chloride was obtained in 54% yield. (b) β-D-*Glucopyranose penta-acetate.* The β-chloride was isolated in 62% yield, and the specific rotation of the syrupy mixture initially obtained indicated a ratio of β-chloride to α-chloride of about 69 : 31. (c) α-D-*Mannopyranose penta-acetate.* The reaction period was 4 days, and α-mannosyl chloride was isolated in 76% yield, no β-chloride being detected at any stage. (d) β-D-*Fructopyranose* 1 : 3 : 4 : 5-*tetra-acetate.* Tetra-*O*-acetyl-β-D-fructopyranosyl chloride was obtained in 76% yield. (e) β-*Lactose octa-acetate and* β-*maltose octa-acetate.* Each afforded the corresponding hepta-*O*-acetyl-α-glycosyl chloride in about 65% yield. (f) *Tetra*-O-*acetyl*-α-D-*glucopyranosyl chloride.* The residue initially obtained on evaporation of the benzene had $[\alpha]_D^{17}$ +150° instead of +174°, but at least 73% of pure α-chloride was recovered.

Stability of Tetra-O-*acetyl*-β-D-*glucopyranosyl Chloride in Solution.*—Thoroughly dried apparatus and purified chloroform, freshly distilled over phosphoric oxide, were used. Solutions containing 1, 2, and 4% (w/v) of the β-chloride were prepared with careful exclusion of moisture, and as far as possible all were handled in the same way. The initial specific rotations were very similar (−7° to −8°), and the rotations were also similar after 24 hr. (+2° to +2·5°), but after one week the specific rotations of the respective solutions were +10·8°, +7·5°, and +2·6°, calculated on the starting material.

In another experiment, a 1% solution of β-chloride was prepared by percolating the dried chloroform through activated aluminium oxide directly into the flask containing the chloride. The neck of the flask was sealed in the flame, and the solution was set aside for 24 hr. The specific rotation changed only from −8° to −4°.

Solutions of β-chloride in less thoroughly dried chloroform, for which the rotational changes were much larger, never afforded crystalline material on evaporation, and the syrups obtained always contained easily ionisable chlorine.

The stability of the β-chloride in the presence of tertiary bases was briefly examined. A solution (1%) of the chloride in a mixture of equal volumes of anhydrous ether and anhydrous collidine showed a change in specific rotation from −23° to −17° during 6 days. In a comparable experiment with pyridine in place of collidine, the change was from −18° to −9° in 19 hr., and to +45° in 7 days.

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129. *Modification of Hudson's Rules of Isorotation for Sugar Derivatives containing Highly Polarisable Aglycones.*

By W. Korytnyk.

Hudson's rotational correlations of glycosyl halides have been critically examined. New A_{Cl} and B_{Cl} values have been calculated from anomeric glycosyl chlorides now available. The presence of a highly polarisable group attached to the reducing centre may cause a change in both A and B values, but constant A values and regular changes in B values have been observed for closely related structures. For (1′ ⟶ 4)- and (1′ ⟶ 6)-linked disaccharides the modification of the B value is apparently confined to the reducing-sugar component, and the modified B value may be evaluated by a simple procedure. Specific rotations calculated for numerous derivatives of disaccharides agree well with reported values; the derivatives include acetylated phenyl glycosides and thioglycosides, and *O*-acetylglycosyl chlorides, bromides, and iodides. The procedure is also applicable to derivatives of monosaccharides. Consideration of structural similarities around the anomeric centres and of the polarisabilities of aglycones allows Hudson's rules of isorotation and the present modifications of them to be rationalised, and their applicability is more closely defined.

Preparation of a series of authentic pairs of poly-*O*-acetyl glycosyl chlorides [1] has permitted a precise test to be made of Hudson's rules of isorotation for the first time in this series. This was impossible in 1924, as only the more stable of the anomeric chlorides derivable from each sugar was then known, and Hudson [2] had to assume the validity of his second rule for the numerous halides he examined. Using the B values (°) (rotational contribution from the ring portion other than the anomeric centre) derived from acetylated sugars, Hudson calculated A values (°) (contribution from the anomeric centre and its substituent) for the different halogens. The A values so obtained showed a reasonable uniformity and Hudson was able to assign configurations (usually α-D) to the known halides. These have been confirmed by subsequent work.[3] He was also able to detect at least one error in published work, revealed by an abnormal A value in his list.[2,4] One further correction may now be made. Hudson [1] observed an abnormal A value (52,200) for tetra-*O*-acetyl-α-D-galactopyranosyl chloride, but it is now known [1] that the value [5] for the specific rotation (212·5°) used by him and accepted for 56 years, is wrong, and the corrected rotation (177·5°) gives an A value (39,700) near to Hudson's average for A_{Cl} (37,800). The only seriously discordant A_{Cl} value left in Hudson's list is therefore that for tetra-*O*-acetyl-α-D-mannopyranosyl chloride, and by 1930 [6] it was apparent that the original rules of isorotation do not hold accurately for compounds with inverted configuration at $C_{(2)}$.

Table 1 gives optical parameters (A and B values) for seven pairs of anomeric glycosyl chlorides, which were determined independently of Hudson's assumption that $B_{Cl} = B_{Ac}$ (the subscripts show the substituent at $C_{(1)}$ in the acetylated sugar to which the B values refer). The new values have been compared with those of fully acetylated sugars. All optical rotations ($[\alpha]_D$ at about 20°) of these and other acetylated derivatives discussed in this paper refer to chloroform solutions, and the unacetylated ones to water solutions, as suggested by Hudson.[2] In all cases the B_{Cl} values differ appreciably from B_{Ac} values, and the A_{Cl} value is similar in only the first four pairs. It is suggested that the A and B values

[1] Korytnyk and Mills, *J.*, preceding paper.
[2] Hudson, *J. Amer. Chem. Soc.*, 1924, **46**, 462.
[3] Haynes and Newth, *Adv. Carbohydrate Chem.*, 1955, **10**, 207.
[4] Hudson and Kunz, *J. Amer. Chem. Soc.*, 1925, **47**, 2052.
[5] Skraup and Kremann, *Monatsh.*, 1901, **22**, 375.
[6] Haworth and Hirst, *J.*, 1930, 2615.

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derived from Hudson's procedure should be designated A'_{Cl} and B'_{Cl} to distinguish them from true values derived from anomers.

Phenyl glycosides are known to differ from alkyl glycosides in not conforming accurately to the original isorotation rules,[7] and Table 2 shows a situation closely resembling that for the chlorides in Table 1.

TABLE 1. *Optical data for anomeric fully acetylated pyranose sugars and corresponding poly-O-acetyl glycosyl chlorides (in chloroform)* (°).

(1) *Molecular rotations,* $[M]_D$, *of anomers* [a]

Parent sugar	Acetylated sugar α-form	Acetylated sugar β-form	Acetylated chloride α-form	Acetylated chloride β-form
D-Glucopyranose	39,700	1,480	60,900	−4,770
Methyl D-glucopyranuronate	36,900 [b]	3,270 [b]	59,700 [c]	−5,900 [b]
D-Galactopyranose	41,650	9,760	65,100 [d]	5,450 [d]
Maltose	83,330	42,500	104,500	37,600 [d]
D-Mannopyranose	21,470	−9,840	32,970	−12,500 [d]
D-*glycero*-D-*gulo*Heptopyranose	40,230	2,220	41,690	4,830
D-Xylopyranose	28,400	−7,860	50,450	−41,600 [d]

(2) *Optical parameters for acetylated derivatives*

Parent sugar	A_{Ac}	B_{Ac}	A_{Cl}	B_{Cl}	A_{Ac}/A_{Cl}	B_{Ac}/B_{Cl}
D-Glucopyranose	19,110	20,590	32,840	28,060	0·58	0·74
Methyl D-glucopyranuronate	16,820	20,080	32,800	26,900	0·51	0·75
D-Galactopyranose	15,950	25,700	29,830	35,280	0·53	0·73
Maltose	20,420	62,920	33,450	71,050	0·61	0·89
D-Mannopyranose	15,660	5,820	22,740	10,240	0·69	0·57
D-*glycero*-D-*gulo*Heptopyranose	19,010	21,230	18,430	23,260	1·0	0·91
D-Xylopyranose	18,130	10,270	46,030	4,430	0·39	2·3

[a] Calculated from the data of ref. 8, unless specified. [b] Goebel and Babers, *J. Biol. Chem.*, 1934, **106**, 63. [c] Ref. 15. [d] Ref. 1.

TABLE 2. *Optical parameters of some fully acetylated phenyl glycosides (in chloroform)* (°).

Acetate of		$[M]_D$	A_{OPh}	B_{OPh}	A_{Ac}/A_{OPh}	B_{Ac}/B_{OPh}
Phenyl D-glucopyranoside	α	71,500 [a]	40,520	30,980	0·47	0·66
	β	−9,540 [a]				
Phenyl D-galactopyranoside	α	74,400 [b]	37,350	37,050	0·43	0·69
	β	−300 [c]				
Phenyl maltoside	α	117,000 [d]	43,500	73,400	0·47	0·86
	β	29,900 [d]				
Phenyl cellobioside	α	59,200 [c]	42,400	16,700	0·45	0·53
	β	−25,700 [c]				
Phenyl D-xylopyranoside	α	47,600 [a]	32,700	14,900	0·55	0·69
	β	−17,800 [a]				

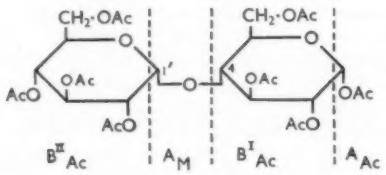
[a] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1942, **64**, 690. [b] Helferich and Bredereck, *Annalen*, 1928, **465**, 166. [c] Helferich and Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 378. [d] Asp and Lindberg, *Acta Chem. Scand.*, 1952, **6**, 941. [e] Ref. 10.

It is evident from both Tables that constant A values are only observed in sugar derivatives that have a similar configuration round positions 1, 2, 3, and 5. A modification of either configuration or structure at positions 4 and 6 appears not to have a marked effect on the A value. Poly-*O*-acetylglycosyl chlorides and phenyl glycosides with a *xylo*- or *gulo*-configuration show discrepancies of their A values, although acetates and methyl glycosides of gulose and xylose seem to conform well to the isorotation rules. It is shown below that the variations in A and B values are due to interactions between polarisable groups at position 1 and the closer portions of the rest of the molecule.

The ratios A_{Ac}/A_{Cl} and B_{Ac}/B_{Cl} are fairly constant for the first three pairs in Table 1, and the corresponding ratios are also similar for the first two pairs of phenyl glycosides in Table 2. The different B_{Ac}/B_{Cl} ratio for maltosyl chlorides in Table 1, and the variable

[7] Bonner, Kubitshek, and Drisco, *J. Amer. Chem. Soc.*, 1952, **74**, 5082.

B_{Ac}/B_{OPh} ratios for phenyl glycosides of disaccharides in Table 2, are due to the fact that B values of these derivatives are composite values for two D-glucopyranose rings, and probably only one ring is close enough to the 1-substituent to suffer modification of its partial B value. For the purpose of evaluating the influence of the phenoxy-group or chlorine atom on the B value of the reducing D-glucopyranose ring, it is proposed to dissect the disaccharide molecule as shown for maltose in (I) and evaluate the contribution of the non-reducing ring, $B^{II}_{Ac} + A_M$, by subtracting the molecular rotation of α-D-glucopyranose penta-acetate from that of α-maltose octa-acetate. Subtracting this value (**43,630**) from B_{Ac} and B_{Cl} for maltose then gives the partial B values for the reducing ring; they are $B^{I}_{Ac} = 19{,}330$, $B^{I}_{Cl} = 26{,}420$, whence $B^{I}_{Ac}/B^{I}_{Cl} = 0{\cdot}73$ in good agreement with the simple sugars. When this method is applied to the acetylated phenyl glycosides of disaccharides in Table 2, B^{I}_{Ac}/B^{I}_{OPh} is found to be 0·65 for maltose and 0·73 for cellobiose.



(I)

As would be expected if the method is sound, the contribution $B^{II}_{Ac} + A_M$ is practically constant when calculated in all possible ways: the values obtained from the β-acetates, α-chlorides, and β-chlorides of maltose and D-glucose are **41,020**, **43,600**, and **42,370**, respectively. The above numerical analysis is equivalent to stating that the difference, $B_{Cl} - B_{Ac} = \Delta B$, is constant for related anomeric pairs of mono- and di-saccharides; for maltose and D-glucose the actual values of ΔB are **8130** and **7470** respectively. If this relation is true in general, it provides a means of calculating the specific rotation of both chlorides of derivatives of D-glucose, provided the substitution is confined to points beyond the modifying influence of the chlorine atom. In particular, the method may be applied to (1′ ⟶ 4)- and (1′ ⟶ 6)-linked disaccharides with D-glucose as the reducing component. The exact relation:

$$[M_{Cl}]^{di} = B_{Cl}{}^{di} \pm A_{Cl}{}^{di}$$

becomes, on these assumptions:

$$[M_{Cl}]^{di} = B_{Ac}{}^{di} + B_{Cl}{}^{mono} - B_{Ac}{}^{mono} \pm A_{Cl}{}^{mono} \quad . \quad . \quad . \quad . \quad (1)$$

$[M_{Cl}]$ indicates the molecular rotation of the chloride, the superscripts indicate mono- or di-saccharide, and the + or − sign is appropriate to the α- or β-anomer, respectively. The success of this method as applied to poly-*O*-acetyldisaccharide chlorides is shown in Table 3. Thus the specific rotation of hepta-*O*-acetyl-β-maltosyl chloride was predicted by Hudson [2] to be 38°; the present method gives 57°, which is in perfect agreement with the found value. An exactly similar method should hold for acetylated phenyl glycosides of these disaccharides, and the appropriate relation is obtained from equation (1) on substituting B_{OPh} and A_{OPh} for D-glucose (Table 2) for $B_{Cl}{}^{mono}$ and $A_{Cl}{}^{mono}$. The results of calculations are also shown in Table 3. The agreement with the known value is as good as could be expected.

If the extent of modification of the B value of the reducing monosaccharide unit is known, it is generally possible to predict rotations of anomeric forms of oligosaccharides, provided the modifying influence of the aglycone does not reach carbon atoms to which the other sugar units are attached.

Thus it should be possible to evaluate the specific rotations (in water) of unacetylated phenyl glycosides by using the parameters derived from methyl glycosides of mono- and

di-saccharides and the phenyl glycosides of the monosaccharide. Unfortunately, the requisite data [8] are scanty and of doubtful quality; the A value for the methyl cellobiosides (20,650) is significantly different from the A values for the methyl gentiobiosides (18,070) and methyl D-glucopyranosides (18,750). By use of the data for these glycosides and the phenyl D-glucopyranosides,[8] the following rotations were calculated, the reported values being shown in parentheses: phenyl α-cellobioside,[9] 115° (122°); phenyl β-cellobioside,[10]

TABLE 3. *Calculated and reported rotations (in chloroform) for poly-O-acetyl glycosyl chlorides and acetylated phenyl glycosides of some disaccharides.*

		Maltose $[\alpha]_D$	Melibiose $[\alpha]_D$	Lactose $[\alpha]_D$	Gentiobiose $[\alpha]_D$	Cellobiose $[\alpha]_D$
α-Chloride	calc.	157°	197°	87°	86°	75°
	found [a]	159	192·5	84	80·5	72
β-Chloride	calc.	57	97	−13	−14	−25
	found	57 [b]	*g*	*g*	*g*	*g*
Phenyl α-glycoside	calc.	160	196	95	94	84
	found	164 [c]	*g*	*g*	*g*	83 [e]
Phenyl β-glycoside	calc.	46	82	−19	−20	−30
	found	42 [c]	*g*	−23 [d]	−29 [e]	−36 [f]
Parameters used						
B_{Ac} (known) [h]		62,960	88,670	16,600	16,000	8,900
B_{Cl} (calc.)		70,430	96,140	24,070	23,470	16,370
B_{OPh} (calc.)		73,350	99,080	26,990	26,390	19,290

[a] Unless specified, reported rotations are from ref. 8. [b] Ref. 1. [c] Asp and Lindberg, *Acta Chem. Scand.*, 1952, **6**, 941. [d] Helferich and Griebel, *Annalen*, 1940, **544**, 191. [e] Ref. 11. [f] Ref. 10. [g] Compound not known. [h] Calc. from data in ref. 8.

−40° (−59·5°); and phenyl β-gentiobioside,[11] −60° (−67°). Further study of this series is necessary, to find whether the rather less satisfactory agreement is due to inaccurate parameters, or to the possibly greater anomalies in water as solvent.

If equation (1) is expressed in general terms, for an aglycone X, it may be reduced to:

$$[M_X]^{di} - B_{Ac}{}^{di} = [M_X]^{mono} - B_{Ac}{}^{mono} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and have the same validity, provided A_X is constant and the molecular rotations refer to derivatives of the *same* anomeric configuration. This implies that if one α-anomer containing X is known, and the appropriate B_{Ac} values are available, it is possible to calculate the rotations of other α-anomers with substituent X in the series without having any β-anomers available, and conversely for a series of β-anomers. Equation (2) may be used for the foregoing calculations made from equation (1), and gives identical results. The validity of equation (2) was checked for the following series, in which only one anomeric form of the derivative is known for each sugar; the calculated specific rotations are shown, with reported values in parentheses.

(*a*) Acetylated phenyl thioglycosides (β-forms): [12,13] cellobiose, −27° (−28·5°); lactose, −16° (−19·6°); maltose, 48° (49·0°). Specific rotations of acetylated 2′-naphthyl-1-thio-β-D-glucopyranosides [14] can also be predicted with a similar degree of accuracy.

(*b*) Poly-*O*-acetylglycosyl bromides (α-forms): [8] cellobiose 100° (95·8°); gentiobiose, 110° (101·1°); lactose 111° (108·7°); maltose 177° (180·1°); melibiose 214° (209·9°).

(*c*) Poly-*O*-acetylglycosyl iodides (α-forms): [8] cellobiose, 130° (125·7°); gentiobiose, 140° (126·1°); lactose, 141° (136·9°).

[8] Bates and associates, " Polarimetry, Saccharimetry and the Sugars," U.S. Government Printing Office, Washington, 1942, Tables, pp. 704 *et seq.*
[9] Stanek and Kocourek, *Chem. Listy*, 1953, **47**, 697 (*Chem. Abs.*, 1955, **49**, 190).
[10] Montgomery, Richtmyer, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 1848.
[11] Helferich and Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 383.
[12] Purves, *J. Amer. Chem. Soc.*, 1929, **51**, 3619.
[13] *Idem, ibid.*, p. 3631.
[14] Haskins, Hann, and Hudson, *ibid.*, 1947, **69**, 1668.

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The fair success achieved by Hudson in his analysis of the rotation of *O*-acetylglycosyl halides and other derivatives which are known (or would be expected) not to conform to his rule of isorotation, is now explicable. His A'_{Cl} values are in fact $[M_{Cl}] - B_{Ac}$, and his assumption that A'_{Cl} is constant was fully justified for all derivatives of D-glucose for which the relation (2) is now shown to hold with numerical accuracy, and also for sugars such as D-galactose in which changes are made outside the range of the vicinal action of the chlorine atom. For the same sugars, the ratio B_{Ac}/B_{Cl} is nearly constant; therefore, although Hudson's A_{Cl} and B_{Cl} values were wrong, they were wrong in a constant ratio for the majority of sugars he examined, and therefore self-consistent. Calculation of A'_X values for Goebel and Babers's methyl 2 : 3 : 4-tri-*O*-acetyl-1-chloro-1-deoxy-α-D-glucopyranuronate [15] ($A'_{Cl} = 39{,}600$) and the corresponding 1-bromo-derivative [15] ($A'_{Br} = 58{,}500$) gives results very close to the mean values for A'_{Cl} (37,800) and A'_{Br} (59,300) as determined by Hudson [2] for structurally similar α-D-halides, and this strongly confirms the α-D-configuration of these derivatives. The more serious discrepancies are found in his data for such sugars as D-mannose, in which changes are made close to the anomeric centre.

Hudson's method could not lead to accurate predicted rotations for the unknown β-chlorides, because the modification of the B value by the chlorine requires at least one β-chloride as a starting point for the β-series. Hudson's predicted rotation [2] of $[\alpha]_D$ −42° for tetra-*O*-acetyl-β-D-glucopyranosyl chloride differed from that found [16] for " β-acetochloroglucose " shortly after, and the discrepancy has been used as an argument for the reassignment of structure to the latter compound.[17]

The present analysis can also be successfully applied to some derivatives of D-mannose. Knowledge of rotational parameters of tetra-*O*-acetyl-D-mannopyranosyl chlorides (Table 1) allows the calculation of specific rotations of hepta-*O*-acetyl-4-*O*-(β-D-glucopyranosyl)-D-mannopyranosyl chlorides by equation (1); the calculated values are 53·5° for the α-anomer (Brauns [18] found 51·2°) and −16° for the β-anomer (not known). By means of equation (2) the following values have been calculated for the other acetylated α-halides of this disaccharide (found values [8,18] in parentheses): fluoride, 15° (13·6°); bromide, 80° (77·9°); and iodide, 119° (111·5°).

The calculations may be simplified without serious error when the 4- and the 6-substituent do not contain an asymmetric centre, as B_{Ac} values are not then required. To get the B_{Cl} value for the derivative, the B_{Cl} value for the parent acetylated sugar is multiplied by the factor required to compensate for the change of molecular weight caused by substitution. For example, the molecular weight of the " basal chain " or ring in tetra-*O*-acetyl-D-glucopyranosyl chloride is 331, and in the corresponding tri-*O*-acetyl-6-*O*-tosyl derivative is 443. The B_{Cl} value for the parent compound is 28,060, therefore this is multiplied by 443/331 to get the B_{Cl} value (37,600) for the 6-*O*-tosyl derivative. Combined with the A_{Cl} value of D-glucose (32,840) this gives a calculated specific rotation of 10° for 2 : 3 : 4-tri-*O*-acetyl-6-*O*-tosyl-β-D-glucopyranosyl chloride; the measured value [1] is 9°.

Useful information may sometimes be obtained even when anomeric pairs of acetates and glycosyl halides are not available, as is shown in the following calculation of the specific rotation of 2 : 3-di-*O*-acetyl-4 : 6-*O*-benzylidene-β-D-glucopyranosyl chloride. Only one form of 4 : 6-*O*-benzylidene-D-glucose triacetate is known, for which a β-configuration is indicated by the method of preparation and its conversion into a glycosyl chloride by aluminium chloride under mild conditions.[1] The modification of the D-glucose molecule in the benzylidene derivative is confined to $C_{(4)}$ and $C_{(6)}$; therefore A_{Ac} for the benzylidene triacetate and A_{Cl} for the benzylidene chloride should be very similar to A_{Ac} and A_{Cl} for D-glucopyranose itself; therefore, $A_{Cl} = 32{,}840$ is adopted for calculations on the

[15] Goebel and Babers, *J. Biol. Chem.*, 1935, **111**, 347.
[16] Schlubach, *Ber.*, 1926, **59**, 840.
[17] Zemplen, Mester, and Eckhart, *Acta Chim. Acad. Sci. Hung.*, 1954, **4**, 73.
[18] Brauns, *J. Amer. Chem. Soc.*, 1926, **48**, 2770.

benzylidene chloride. Calculation of the B_{Ac} value for the benzylidene derivatives from the molecular rotation (−20,400) of 4 : 6-*O*-benzylidene-β-D-glucopyranose triacetate and A_{Ac} for D-glucopyranose gives $B_{Ac} = -1290$. A check is available in a calculation of the B value from the known anomeric forms [19] of methyl 2 : 3-di-*O*-acetyl-4 : 6-*O*-benzylidene-D-glucopyranoside; for these, $B_{OMe} = -2800$, and this should be very close to the true B_{Ac} value. The factor by which B_{Ac} has to be modified to get B_{Cl} for the benzylidene derivative is unknown, but fortunately the postulated B_{Ac} value is very small compared with the postulated A_{Cl} value (32,840), and it may be assumed that $B_{Cl} = B_{Ac} = -1290$ without risk of serious error. The specific rotation of 2 : 3-di-*O*-acetyl-4 : 6-*O*-benzylidene-β-D-glucopyranosyl chloride calculated from the A_{Cl} and B_{Cl} values obtained by this series of approximations is −92°, which agrees closely with the measured value (−89·2°) for the known compound.[1] Good agreement is also obtained in analogous calculations for the corresponding 4 : 6-*O*-ethylidene derivatives; [1] for these, the calculated $B_{Ac} = 9540$, giving a calculated specific rotation for 2 : 3-di-*O*-acetyl-4 : 6-*O*-ethylidene-β-D-glucopyranosyl chloride of −76·5°, comparable with a reported value [1] of −70·5°. If A_{Cl} for glucose applies accurately for these compounds the ratio B_{Ac}/B_{Cl} seems to be about 0·85, and the assumption that $B_{Cl} = B_{Ac}$ was quite safe. A usable correlation would have been obtained even if the ratio had departed much further from unity. The optical correlations confirm the β-configurations assigned on chemical grounds [1] to these 4 : 6-acetals of D-glucose.

The above results show that surprisingly accurate predictions of optical rotations may be made, by using equation (1) or (2), for several classes of carbohydrate derivative to which Hudson's rules of isorotation were formerly thought not to apply with numerical accuracy. For (1′ → 4)- and (1′ → 6)-linked oligosaccharides derived from D-glucose and D-mannose the predicted specific rotations of the acetylated derivatives should be in error by not more than 10°, and often by not more than 5°. Disaccharides have been chosen as illustrations, but the method should apply to other derivatives of (say) D-glucopyranose modified at position 6 or 4 by replacement of an acetoxy-group by alkoxyl or another acyl group, or, probably, by halogen. Specific rotations calculated for 2 : 3 : 4-tri-*O*-acetyl-6-bromo-6-deoxy-α-D-glucopyranosyl bromide and 2 : 3 : 4-tri-*O*-acetyl-6-chloro-6-deoxy-α-D-glucopyranosyl chloride are 199° and 187°, the reported values being 191·4° and 196·8°, respectively.[20,21]

TABLE 4. *Constancy of* B*-values on interchange of " aglycones " of moderate polarisability in acetylated and unacetylated* D*-glucopyranose rings.*

		Acetylated derivative [a, c]			Unacetylated derivative [b]		
Substituent		$[M]_D$	A	B	$[M]_D$	A	B
1-*O*-Methyl	α	47,280	26,930	20,340	30,860	18,750	12,110
	β	−6,590			−6,640		
1-*O*-Ethyl	α	49,700 [d]	29,120	20,580	31,600 [d]	19,620	11,980
	β	−8,540 [d]			−7,640 [d]		
1-*O*-*cyclo*Hexyl	α	52,330 [e]	31,270	21,050	34,900 [e]	22,870	12,070
	β	−10,230 [e]			−10,850 [f]		
1-*O*-Acetyl	α	39,700	19,110	20,590			
	β	1,480					
1-*O*-Benzoyl	α	51,300 [g]	32,650	19,650			
	β	−12,000					

[a] In chloroform. [b] In water. [c] Unless specified, data are from ref. 8. [d] Ferguson, *J. Amer. Chem. Soc.*, **1932**, **54**, 4086. [e] Pascu, *ibid.*, 1930, **52**, 2568. [f] Fischer and Helferich, *Annalen*, 1911, **383**, 68. [g] Fischer and Bergmann, *Ber.*, 1918, **51**, 1760.

These regularities may be rationalised by considering the basis of the rules of isorotation. For the rules to be strictly accurate in the original form, and applicable to a series of

[19] Mathers and Robertson, *J.*, 1933, 696.
[20] Karrer and Smirnoff, *Helv. Chim. Acta*, 1922, **5**, 124.
[21] Helferich and Bredereck, *Ber.*, 1927, **60**, 1995.

anomeric pairs of carbohydrates, two alternative conditions must be satisfied: (*a*) There should be no interaction between the anomeric centre and its substituent, $C_{(1)}$–X, and the rest of the molecule. In this case van't Hoff's principle of optical superposition would hold exactly. (*b*) There should be a strictly comparable interaction between $C_{(1)}$–X and the rest of the molecule if the structural environment around $C_{(1)}$ is similar and X is either the same group or has similar electronic properties. It is the latter condition which is applicable in carbohydrates, and to which regularities in steroids and terpenoids [22] have been ascribed. A departure from condition (*b*) leads to irregular A and B values. The most probable source of electronic interactions between the anomeric substituent and the rest of the molecule is the polarisability of the $C_{(1)}$–X bond. Interchange of aglycones, which may show considerable variations in the A value, leaves the B value unaltered, as required by the second isorotation rule, only when the " aglycone " is of low or moderate polarisability. This is illustrated by the data for various acetylated and free alkyl D-glucopyranosides in Table 4, which should be compared with the data for glucose in Tables 1 and 2. The polarisability of the C–F bond is fairly low,[23] and it is not surprising to find for two known pairs of anomeric acetylated glycosyl fluorides that the B value is not greatly altered by the presence of the fluorine atom: for α- and β-tetra-*O*-acetyl-D-glucopyranosyl fluorides,[24] $B_F = 19{,}640$, and for the D-glucose penta-acetates (Table 1), $B_{Ac} = 20{,}590$; and for the corresponding anomeric derivatives of 6-bromo-6-deoxy-D-glucose, $B_F = 25{,}900$ for the fluorides,[25] and $B_{Ac} = 25{,}190$ for the acetates.[26]

If the aglycone is of low or moderate polarisability, its A value remains fairly constant, as required by the first isorotation rule, even if marked changes occur at positions 3 and 5. Only changes at position 2 appear to have an effect on the A values of all aglycones; therefore the vicinal action of the $C_{(1)}$–X group always extends at least as far as $C_{(2)}$.

The vicinal action of the more readily polarisable groups at position 1, such as chlorine, phenoxy, phenylthio, and probably bromine and iodine, but not fluorine, extends further, embracing at least position 5 and probably position 3, so that an exact correspondence of structure is required over this part of the molecule to obtain concordant optical parameters. The interaction causes a modification of A and B values, the extent of which is determined by the nature of the aglycone. Considerable latitude is still permissible in structural changes at the most distant parts, positions 4 and 6, without causing further changes in A values or irregularities in B values. Close correspondence of conformation will also be required over the whole molecule, and in fact in all compounds discussed the pyranose rings have stable C1 conformations. The same considerations would apply for mannopyranose derivatives, for which conformational differences have been postulated to cause irregularities of optical rotations.[27]

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[22] Mills, *J.*, 1952, 4976.
[23] Remick, " Electronic Interpretations of Organic Chemistry," 2nd edn., John Wiley and Sons, New York, 1949, p. 94.
[24] Brauns, *J. Amer. Chem. Soc.*, 1923, **45**, 833; Helferich and Gootz, *Ber.*, 1929, **62**, 2505.
[25] Micheel, *Chem. Ber.*, 1957, **90**, 1612.
[26] Helferich and Himmen, *Ber.*, 1928, **61**, 1825; Fischer, Helferich, and Ostmann, *Ber.*, 1920, **53**, 873.
[27] Pacsu, *J. Amer. Chem. Soc.*, 1939, **61**, 2669; Hudson, *ibid.*, 1939, **61**, 2972.

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130. *Infrared Absorption of Heteroaromatic, Five-membered, Monocyclic Nuclei. Part I. 2-Monosubstituted Furans.*

By A. R. Katritzky and (Mrs.) J. M. Lagowski.

The positions and intensities of nine characteristic infrared bands are recorded and discussed for twenty-four 2-monosubstituted furans.

All the infrared bands ($\varepsilon_A \geqslant 15$), with few exceptions, for monosubstituted benzenes, pyridines, and pyridine 1-oxides are characteristic of either the substituent or the nucleus. Further, any one nucleus (or substituent) shows a characteristic number of bands, the positions and intensities of which are either reasonably constant or vary with the electronic nature of the substituent (or nucleus);[1] mass effects are small, provided that substituents are attached to the nucleus by a carbon, nitrogen, or oxygen atom. We are now investigating five-membered heteroaromatic compounds; this paper describes the results for 2-substituted furans. For reasons given previously,[1a] the spectra of 0·179M-chloroform solutions were measured in a 0·112 mm. compensated cell and apparent molecular extinction coefficients recorded; the errors and approximations involved are noted in ref. 1*a*. Of the bands with $\varepsilon_A \geqslant 15$ between 2000 and 800 cm.$^{-1}$, nine were found to be characteristic of the nucleus and are recorded in Table 1.

The normal vibrations of six-membered heteroaromatic nuclei can be divided into those involving mainly (*a*) C–H stretching near 3000 cm.$^{-1}$, (*b*) C–C and C–(hetero-atom) stretching at *ca.* 1600—1400 cm.$^{-1}$, (*c*) CH in-plane deformation near 1300—1000 cm.$^{-1}$, (*d*) CH out-of-plane deformation at *ca.* 900—700 cm.$^{-1}$, (*e*) ring deformation below 700 cm.$^{-1}$, and (*f*) ring breathing (intermediate between stretching and deformation) near 1000 cm.$^{-1}$. Previous work [2,3] indicates that the normal vibrations of pyrrole, furan, and thiophen can also be so classified, usually with similar ranges for each vibration type: type *a* occurs near 3000 cm.$^{-1}$, type *b* at 1590—1358 cm.$^{-1}$, type *c* at 1270—1015 cm.$^{-1}$ (except that one of the B_1 vibrations in this class apparently absorbs at 872 cm.$^{-1}$ for both thiophen and furan), type *d* at 869—711 cm.$^{-1}$ (a band at 1046 cm.$^{-1}$ for pyrrole is a doubtful exception [2]), and type *e* below 838 cm.$^{-1}$ (all but one lie below 724 cm.$^{-1}$), although the ring breathing vibration (type *f*) causes absorption at 1144, 994, and 832 cm.$^{-1}$ for pyrrole, furan, and thiophen, respectively. Chloroform absorption below 800 cm.$^{-1}$ obscures all vibrations of type *e* and some of type *d*. The sodium chloride prism used did not allow good resolution of type *a* vibrations. This paper is concerned with ring stretching and breathing and CH in- and out-of-plane deformation frequencies.

Ring Stretching Frequencies at ca. 1600—1400 *cm.*$^{-1}$.—Under our conditions, furan shows bands at 1590 cm.$^{-1}$ (10),* 1487 cm.$^{-1}$ (60), and 1381 cm.$^{-1}$ (25). Thompson and

(I) (II) (III) (IV)

Temple [3] assigned these to the normal modes (I—III) (ν_{15}, ν_6, and ν_5 in the notation of Lord and Miller [2]), respectively. A fourth normal mode (IV; ν_{14}) is expected, but not found, in this region.

For six-membered ring compounds, substituents affect the position of bands of this

* Apparent extinction coefficients are in parentheses, and arithmetical means and standard deviations in brackets (see ref. 1*a*). The intensities of shoulders and superimposed bands and the positions of shoulders are not treated statistically.

[1] Katritzky and his co-workers, *J.*, 1958, (*a*) 2182, (*b*) 2192, (*c*) 2195, (*d*) 2198, (*e*) 2202, (*f*) 3165, (*g*) 4155, (*h*) 4162, (*i*) unpublished work.
[2] Lord and Miller, *J. Chem. Phys.*, 1942, **10**, 328.
[3] Thompson and Temple, *Trans. Faraday Soc.*, 1945, **41**, 27.

TABLE 1.

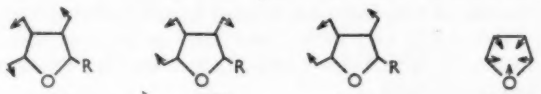
No.	Subst.	1 B_1 νC=C / νC=O		2 A_1 νC=C / νC=O		3 A_1 νC=C / νC=O		4 B_1 βCH		5 A_1 βCH		6 A_1 ring breath		7 B_2 γCH		8 A_2 γCH		9 B_2 γCH		10	11	12
		cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	cm.$^{-1}$	ε_A	B. p.	mm.	Ref.
1	Me	1607	30	1512	40	1390	15	1145	95	1076	35	1013	85	912	90	882	15	—		65°	760	*a*
2	$CH_2{\cdot}CH_2{\cdot}CO_2Bu^n$	1602	25	1509	20	(—)		1151‡	130	1077	50	1010	60	922	40	883	25	—		118—119	14	*b*
3	$CH_2{\cdot}CH_2{\cdot}CO_2Pr^n$	1605	25	1511	25	(—)		1154‡	125	1079	60	1012	95	924	40	885	30	—		115—116	17	*c*
4	$CH_2{\cdot}CH_2{\cdot}CO_2Et$	1603	20	1511	25	(—)		1155‡	125	1079	55	1017	90	925	35	885	20	—		108	17	*d*
5	$CH_2{\cdot}CH_2{\cdot}CO_2Me$	1602	20	1510	20	(—)		1155‡	100	1078	45	1014	70	924	25	887	15	—		90	14	*e*
6	$CH_2{\cdot}NH_2$	1605	20	1510	30	1377	15	1151	90	1072	30	1010	100	920	50	885‡	100	—		144—145	760	*a*
7	$CH_2{\cdot}OH$	1605	10	1507	35	1381‡	50	1151	110	1078	25	(—)		912	60	886	40	—		73·5	15	*a*
8	$CH_2{\cdot}O{\cdot}COMe$	1611	10	1506	40	1395*	25	1152	120	1078	25	1013‡	190	916	90	882	50	810	50	74	14	*f*
9	$CH{:}CH{\cdot}CO_2Bu^n$	1563	45	1484	75	1393‡	80	(—)		1075	55	1016	280	927	60	882	120	811	55	147	14	*g*
10	$CH{:}CH{\cdot}CO_2Pr^n$	1563	50	1482	75	1394‡	85	(—)		1075	45	1016	260	927‡	75	882	120	811	60	113	16	*a*
11	$CH{:}CH{\cdot}CO_2Et$	1560	55	1484	85	1393‡	60	(—)		1076	45	1018	270	927	45	884	80	810	40	124	22	*a*
12	$CH{:}CH{\cdot}CO_2Me$	1562	55	1485	70	1392	35	(—)		1078	35	1020	260	930	65	885	80	812	40	117	23	*a*
13	$CH{:}CH{\cdot}COMe$	1558	135	1480	70	1392	60	1172	80	1077	20	1016	245	926	55	881	130	803	40	113	14	*h*
14	$CH{:}N{\cdot}OH$	—		1494	30	1383	40	1156	90	1075	15	1018	100	931	165	885	65	—		74—75	*i*	*a*
15	$CMe{:}N{\cdot}OH$	—		1498	35	1395	50	1167	110	1073	5	1006	180	942	90	(—)		—		104	*i*	*a*
16	$CH{:}N{\cdot}NHPh$	(—)		1485*	90	1387	5	1156	130	1069‡	95	1017	120	936	50	884	100	—		95—96	*i*	*a*
17	$CMe{:}N{\cdot}NHPh$	(—)		1480*	65	1388	20	1164	135	1071	75	1022	110	910	65	883	75	—		85—86	*i*	*a*
18	C$\equiv$N	1583	5	1478	75	1384	10	1153	65	1074	45	1017	150	926	50	886	35	829	25	146—147	760	*j*
19	CO_2Bu^n	1587 1576*	85 65	1482	150	1404	105	1174*	185	1076	70	1012	140	939	60	884	100	836‡ 813*	20 15	117	20	*a*
20	CO_2Pr^n	1585 1574*	100 70	1478	180	1405	110	1174*	165	1076	70	1013	180	945	60	883	110	835	15	112	20	*a*
21	CO_2Et	1585 1575*	85 55	1483	155	1405	95	(—)		1076	75	1010	180	932	70	884	90	837 821	15 10	84—85	16	*k*
22	CO_2Me	1585 1574	100 60	1485	175	1396	100	1169	150	1079	55	1017	95	910	55	886	75	837‡	10	90·5	55	*k*
23	CHO	1573	95	1470	180	1398	115	1161	55	1084	40	1021	190	930	55	884	60	835	20	52·5	12	*a*
24	CO·Me	1575	145	1474	290	1400	105	1173 1166	65 70	1074	20	1025 1013	110 75	917	40	886	85	834	20	66	13	*a*

TABLE 2.

Substituent Type	Nos.	B_1 Band near 1600 cm.$^{-1}$ Position (cm.$^{-1}$) Range	Position (cm.$^{-1}$) Statistics	Intensity (ε_A) Range	Intensity (ε_A) Statistics	A_1 Band near 1500 cm.$^{-1}$ Position (cm.$^{-1}$) Range	Position (cm.$^{-1}$) Statistics	Intensity (ε_A) Range	Intensity (ε_A) Statistics	A_1 Band near 1400 cm.$^{-1}$ Position (cm.$^{-1}$) Range	Position (cm.$^{-1}$) Statistics	Intensity (ε_A) Range	Intensity (ε_A) Statistics
H	—	1590	—	10	—	1487	—	60	—	1381	—	25	—
Sat. C	1—8	1611—1602	1605 ± 3	10—30	20 ± 7	1512—1506	1510 ± 2	20—40	30 ± 8	1390—1377	1383 ± 7	15	—
C:C	9—13	1563—1558	1561 ± 2	45—135	65 ± 30	1485—1480	1483 ± 2	70—85	75 ± 5	1394—1392	1393 ± 1	35—60	50 ± 18
C:N	14—18	1583	—	10	—	1498—1478	1490 ± 11	30—75	45 ± 25	1395—1383	1387 ± 5	5—50	25 ± 20
C:O	19—24	1587—1573	1581 ± 6	85—145	100 ± 22	1485—1470	1479 ± 6	150—290	190 ± 50	1405—1396	1401 ± 4	95—115	105 ± 10

type relatively little, but the intensities are considerably changed by substituents which conjugate strongly with the ring.[1] The bands shown by the 2-substituted furan nucleus at 1611—1558, 1512—1470, and 1405—1377 cm.$^{-1}$ (5—145, 20—290, and 15—110) (Table 1, cols. 1—3) are therefore assigned to modes (I—III). The furan ring is a strong electron-donor, and, generally, the band intensities increase with increasing electron-attracting power of the substituent (Table 2). This is as expected, because increased disturbance of the π-electron system gives steep charge gradients and therefore large dipole-moment changes during the vibrations (cf. ref. 1*h*).

Hydrogen In-plane Deformations at 1200—1050 *cm.*$^{-1}$.—In the six-membered ring series, the number and relative orientations of the hydrogen atoms determine the positions of the in- and out-of-plane deformation modes.[1] A five-membered ring with three adjacent hydrogen atoms will show three in-plane and three out-of-plane deformation modes, which, by analogy, should resemble those of vicinal trisubstituted benzenes. All the 2-substituted furans absorb at 1240—1200 cm.$^{-1}$ (positions and intensities cannot be measured since this region is obscured by solvent absorption), 1173—1145 cm.$^{-1}$ (55—135) [1158 ± 7 cm.$^{-1}$ (95 ± 25)] * (overlap raises No. 22's intensity), and 1084—1069 cm.$^{-1}$ (5—75) [1076 ± 3 cm.$^{-1}$ (45 ± 20)] (Table 1, cols. 4 and 5). These bands probably correspond to the three in-plane CH deformations (V—VII). Vibration modes corresponding to (VI) and (VII) for vicinal trisubstituted benzenes absorb at 1160 ± 5 and 1073 ± 10 cm.$^{-1}$; the mode corresponding to (V), which should absorb at somewhat higher frequencies, was not found.[4]



(V) (VI) (VII) (VIII)

Ring Breathing Frequency near 1000 *cm.*$^{-1}$ (*Table* 1, *col.* 6).—The band at 990 cm.$^{-1}$ (170) for furan has been assigned to mode (VIII).[3] All the 2-substituted derivatives show a corresponding band at 1025—1006 [1015 ± 4 cm.$^{-1}$]. The intensity (55—280) depends on the substituent type: for saturated carbon atoms (Nos. 1—8) it is (60—100) [(85 ± 15)], for carbon–carbon double bonds (Nos. 9—13) (245—280) [(265 ± 10)], and for carbon–nitrogen and carbon–oxygen multiple bonds (Nos. 14—24) (95—190) [(140 ± 35)].

Hydrogen Out-of-plane Deformations at 950—800 *cm.*$^{-1}$ (*Table* 1, *cols.* 7—9)—All the 2-substituted furans show bands at 945—910 cm.$^{-1}$ (25—90) [925 ± 9 cm.$^{-1}$ (55±17)] (overlap raises No. 14's intensity) and at 887—881 [884 ± 2] cm.$^{-1}$. The intensity of the latter is (15—50) [(30 ± 13)] for saturated substituents (Nos. 1—8) and (35—130) [(90 ± 20)] for unsaturated ones (Nos. 9—24). Another band is obscured by solvent absorption below 800 cm.$^{-1}$ for saturated substituents but occurs at 812—803 cm.$^{-1}$ (40—60) [809 ± 4 cm.$^{-1}$ (45 ± 10)] for olefins and at 837—834 cm.$^{-1}$ (15—20) [836 ± 1 cm.$^{-1}$ (15 ± 5)] for carbonyl

* See footnote, p. 657.

[4] Randle and Whiffen, Paper No. 12, Report on Conference on Molecular Spectroscopy, 1954. Institute of Petroleum, London.

Footnotes to Table 1:

* Shoulder, ‡ absorption considered to be the superimposition of two peaks, — absence of absorption, (—) band masked by stronger absorption.

[a] "Dictionary of Organic Compounds," edited by Heilbron and Bunbury, Eyre and Spottiswoode, London, 1953. [b] Found: C, 67·7; H, 8·4. $C_{11}H_{16}O_3$ requires C, 67·4; H, 8·2%. n_D^{22} 1·4570. [c] Found: C, 66·2; H, 8·1. $C_{10}H_{14}O_3$ requires C, 66·5; H, 7·7%. $n_D^{22.5}$ 1·4618. [d] Kametani, Ito, and Isaka, *J. Pharm. Soc. Japan*, 1954, **74**, 1298; *Chem. Abs.*, 1955, **49**, 15896c. [e] Sherlin, Berlin, Serebrennikova, and Rabinovich, *J. Gen. Chem.* (*U.S.S.R.*), 1938, **8**, 7; *Chem. Abs.*, 1938, **32**, 5397. [f] *Org. Synth.*, Coll. Vol. I, 1944, p. 285. [g] G.P. 851,064; *Chem. Abs.*, 1956, **50**, 8738e. [h] *Org. Synth.*, *op. cit.*, p. 283. [i] These compounds are solids, and m. p. are given. [j] Hughes and Johnson, *J. Amer. Chem. Soc.*, 1931, **53**, 744. [k] Gennari, *Gazzetta*, 1894, **24**, 249.

The approximate symmetry type is given beneath the column number, those in cols. 1—3 and 6 by analogy with unsubstituted furan, and those in cols. 4—5 and 7—10 by analogy with vicinal trisubstituted benzenes; see text.

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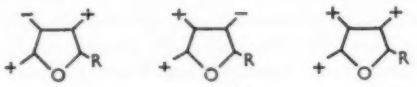
compounds. These bands probably correspond to modes (IX—XI). The modes analogous to (IX—XI) for vicinal trisubstituted benzenes absorb at 958 ± 8 (w), 893 ± 7 (w), and 770 ± 8 cm.$^{-1}$ (vs), respectively.[4]



(IX) (X) (XI)

Substituent Bands.—With few exceptions, all the remaining bands with $\varepsilon_A \geqslant 15$ could be assigned to substituent absorption (cf. ref. 1*a*).

Other Infrared Work.—Early work is summarised in ref. 5. For five 2-monosubstituted furans, Cross, Stevens, and Watts [5] reported bands at 1248—1218, 1021—1010, 941—918, 889—878, and 763—726 cm.$^{-1}$ (the first and last would be obscured by solvent in our work; the others correspond to the bands in Table 1, cols. 6—8). They assigned the band at 1248—1218 cm.$^{-1}$ for 2-monosubstituted furans and that at 1180 cm.$^{-1}$ for furan to the " asymmetrical C–O–C stretch," *i.e.*, presumably to mode (IV). Although the 1180 cm.$^{-1}$ band for furan is probably of this symmetry type (B_1),[3] mode (IV) absorbs at 1418 cm.$^{-1}$ for pyrrole,[2] and a large shift in position seems unlikely. The band at 1021—1010 cm.$^{-1}$ was assigned to the " symmetrical C–O–C stretch;" " ring breathing " is a more conventional description of mode (VIII). Since the completion of the present work, Daasch [6] has published the spectra of four monosubstituted furans and suggested bands at 1597—1565, 1488—1466, 1180—1125, and 1070—1060 cm.$^{-1}$ as possible additional correlations (these correspond to the bands in Table 1, cols. 1, 2, 4, and 5); Cross and Watts [7] accept only the first of these correlations.

Related Raman Work.—Han and others [8,9] recorded the Raman spectra of some 2-monosubstituted furans and noted that several bands were characteristic of this nucleus; no assignment of the modes was attempted. We have now treated statistically the available data for the compounds with the following substituents: Me, $CH_2{\cdot}CH_2{\cdot}CO_2Et$, $CH_2{\cdot}CH_2{\cdot}CO_2Me$, $CH_2{\cdot}CH_2{\cdot}COMe$, $CH_2{\cdot}OMe$, $CH_2{\cdot}OEt$, $CH_2{\cdot}O{\cdot}COMe$, $CH_2{\cdot}OH$, $CH_2{\cdot}NH_2$, $CH{:}CH_2$, $CH{:}CH{\cdot}CO_2Et$, $CH{:}CH{\cdot}CO_2Me$, CN, CO_2Et, CO_2Me, CHO. The three ring stretching frequencies are shown at 1605—1566 cm.$^{-1}$ (s), 1511—1471 cm.$^{-1}$ (vs), and [1388 ± 4] cm.$^{-1}$ (s); the positions of the first two bands are higher for saturated carbon substituents than for substituents capable of accepting electrons, as in the infrared spectra, but the third band is relatively constant in position.

The three CH in-plane deformation modes, the ring breathing mode, and the first two out-of-plane CH deformation modes occur at [1225 ± 10 (m), 1153 ± 10 (m), and 1079 ± 4 (s) cm.$^{-1}$], [1018 ± 4 (m) cm.$^{-1}$], and [926 ± 6 (m) and 885 ± 3 (m) cm.$^{-1}$], respectively; the positions are in good agreement with the infrared spectra. A weak band found for most compounds at 837—761 cm.$^{-1}$ is probably the final CH out-of-plane frequency. Mode (XI) would be expected to absorb weakly in the Raman region.

The Raman data confirm the view that the bands given in Table 1 are fundamentals of the 2-monosubstituted furan ring. Since no other characteristic bands were found in the Raman spectra in the region under consideration, and since there is only a limited number of fundamentals, our assignments are supported.

Experimental.—See refs. 1*a* and 1*g* for conditions of measurement, etc. The compounds, commercial products or prepared by standard methods, were redistilled or recrystallised immediately before measurement.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, September 26th,* 1958.]

[5] Cross, Stevens, and Watts, *J. Appl. Chem.*, 1957, **7**, 562.
[6] Daasch, *Chem. and Ind.*, 1958, 1113.
[7] Cross and Watts, *ibid.*, 1958, 1161.
[8] Matsuno and Han, *Bull. Chem. Soc. Japan*, 1934, **9**, 327; 1937, **12**, 155; Han, *ibid.*, 1936, **11**, 701.
[9] Bonino and Manzoni-Ansidei, *Z. phys. Chem.*, 1934, *B*, **25**, 327.

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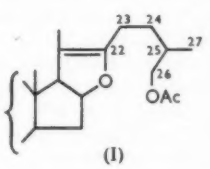
131. *Intermediates for the Synthesis of Optically Active Methyl-substituted Long-chain Acids. Part IV.**

By A. S. Bailey, V. D. Brice, M. G. Horne, and N. Polgar.

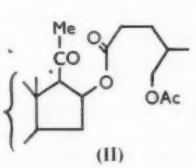
Synthetical studies starting from *L*-(+)-5-acetoxy-4-methylpentanoic acid † (IV), an industrial by-product, are reported.

Model experiments involving the synthesis of 2(*DL*) : 4(*L*)-dimethyldocosanoic acid (VII) with *L*-(−)-3-methylheneicosanoic acid (VI; R = H) as intermediate are also described.

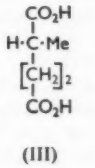
Degradation of sapogenins in industrial syntheses of steroids (cf. ref. 1) yields, as by-products, optically active methyl-substituted acids which contain the asymmetric carbon atom $C_{(25)}$ of the parent sapogenin. We are grateful to Dr. A. G. Long, of Glaxo Laboratories Ltd., for drawing our attention to these degradation products and their possible use for syntheses of optically active methyl-substituted long-chain compounds. This paper reports preliminary experiments with an optically active acid, kindly provided by Glaxo Laboratories Ltd., which was obtained from hecogenin *via* ψ-hecogenin acetate (I) by oxidation with chromic acid, followed by hydrolysis of the resulting ester (II) as described by Cameron *et al.*[1] Hecogenin yields [2] on oxidation of the corresponding *pseudo*-compound an acidic fraction containing carbon atoms $C_{(22)}$ to $C_{(27)}$ inclusive as *D*-(−)-α-methylglutaric acid (III). The acid (found to be dextrorotatory) which resulted



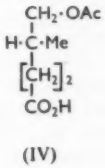
(I)



(II)



(III)



(IV)

on hydrolysis of the ester (II) may, therefore, be expected to have the structure of *L*-(+)-5-acetoxy-4-methylpentanoic acid (IV) (the change of prefix *D* to *L* is due to the conventional alteration of the reference group). This was confirmed by hydrolysis of the acidic material, followed by oxidation with potassium permanganate; the product was identified as (−)-α-methylglutaric acid (III).

For syntheses of long-chain compounds with the acetoxy-acid (IV) as starting material, anodic coupling (cf. ref. 3) with a long-chain acid appeared the most suitable approach. In earlier experiments we investigated the following scheme.

Electrolysis of a mixture of *D*-(−)-(methyl hydrogen β-methylglutarate) [4,5] (V) with stearic acid, followed by hydrolysis of the resulting ester (VI; R = Me), gave *L*-(−)-3-methylheneicosanoic acid (VI; R = H). The silver salt of this acid was degraded with bromine, and the resulting bromide condensed with ethyl methylmalonate, affording 2(*DL*) : 4(*L*)-dimethyldocosanoic acid (VII).

In further experiments we examined the anodic coupling of *L*-(+)-5-acetoxy-4-methylpentanoic acid (IV) with stearic acid. The product, 1-acetoxy-2-methylheneicosane (VIII; R = Ac), resulting from crossed coupling was hydrolysed to *D*-(+)-2-methylheneicosan-1-ol (VIII; R = H). Condensation of the corresponding iodide, obtained *via* the toluene-*p*-sulphonate, with ethyl sodiomethylmalonate afforded, by the usual successive

* Part III, *J.*, 1957, 2934.

† The symbols *D* and *L* are used in the sense defined by Linstead, Lunt, and Weedon (*J.*, 1950, 3333).

[1] Cameron, Evans, Hamlet, Hunt, Jones, and Long, *J.*, 1955, 2807.
[2] James, *J.*, 1955, 637.
[3] Weedon, *Quart. Rev.*, 1952, **6**, 380.
[4] Ställberg-Stenhagen and Stenhagen, *Arkiv Kemi, Min., Geol.*, 1947, **25**, *A*, No. 10.
[5] Linstead, Lunt, and Weedon, *J.*, 1950, 3333.

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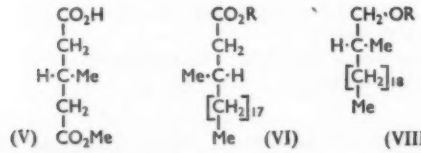
stages (hydrolysis, decarboxylation), 2(*DL*) : 4(*D*)-dimethyltricosanoic acid (IX). In a similar case [6] the 2(*D*)- and the 2(*L*)-diastereoisomer were separable by chromatography of their methyl esters on alumina. Accordingly, on chromatography of the methyl ester of the acid (IX), the fraction more readily eluted yielded a methyl ester of $[\alpha]_D$ −5·1°



(V) (VI) (VIII)

$$Me\text{-}[CH_2]_{17}\text{-}\overset{L}{C}HMe\text{-}CH_2\text{-}\overset{DL}{C}HMe\text{-}CO_2H \quad \text{(VII)}$$

$$Me\text{-}[CH_2]_{18}\text{-}\overset{D}{C}HMe\text{-}CH_2\text{-}\overset{DL}{C}HMe\text{-}CO_2H \quad \text{(IX)}$$

[essentially the 2(*D*)-isomer, the (−)-form of 2-methyl-substituted carboxylic acids having *D*-configuration [7]]; the more strongly absorbed fractions were dextrorotatory. Thus, by using in place of stearic acid a higher homologue with the appropriate chain-length a convenient route is provided for the synthesis of mycoceranic acid.[8]

Experimental

Optical rotations were measured in a 1-dm. tube. Petrol refers to light petroleum, b. p. 40—60°. The alumina used for chromatography was acid-washed, and had activity II on Brockmann and Schodder's scale.[9]

L-(+)-5-*Acetoxy*-4-*methylpentanoic Acid* (IV).—The crude acid, supplied by Glaxo Laboratories Ltd., gave on distillation material, b. p. 167·5°/15 mm., $[\alpha]_D^{20}$ +4·02° (*c*, 14·92 in ether). A 5-g. sample of the latter was hydrolysed with aqueous sodium hydroxide, and the resulting solution oxidised with aqueous 5% potassium permanganate, the mixture being kept below 4°. After filtration, the solution was concentrated, acidified, and extracted with ether. Evaporation of the dried (Na_2SO_4) ethereal extract gave (−)-α-methylglutaric acid, m. p. 81° (from 1 : 1-ether–petrol), $[\alpha]_D^{17\cdot5}$ −21·25° (*c*, 8·37 in water); its p-*bromophenacyl ester* had m. p. 108° (from ethanol) (Found: C, 48·9; H, 3·6; Br, 29·4. $C_{22}H_{20}O_6Br_2$ requires C, 48·9; H, 3·7; Br, 29·6%). Berner and Leonardsen [10] record m. p. 81°, $[\alpha]_D^{20}$ +20·04° (*c*, 7·28 in water), for the (+)-acid.

An authentic specimen of (±)-α-methylglutaric acid, obtained by condensation of ethyl β-iodopropionate with ethyl sodiomethylmalonate, followed by hydrolysis and decarboxylation of the product, had m. p. 76° (from 1 : 1 ether–petrol) (Berner and Leonardsen [10] give m. p. 77°); its *p*-bromophenacyl ester had m. p. 95·5°, after crystallisation from ethanol (Found: C, 49·1; H, 3·9%). For comparison, a 0·7-g. sample of the above (−)-acid was esterified with ethereal diazomethane, and the methyl ester racemised [11] with boiling ethanolic sodium ethoxide (from 1 g. of sodium in 20 c.c. of ethanol) for 4 hr. Aqueous sodium hydroxide (20%; 10 c.c.) was then added, and the mixture refluxed for 2 hr., then concentrated to about half its volume and acidified with hydrochloric acid. Ether-extraction afforded (±)-α-methylglutaric acid, m. p. 76° (from 1 : 1 ether–petrol), which formed a *p*-bromophenacyl ester of m. p. 95·5° (from ethanol); the m. p.s were undepressed on admixture with the authentic specimens.

D-(+)-2-*Methylheneicosan*-1-*ol* (VIII; R = H).—*L*-(+)-5-Acetoxy-4-methylpentanoic acid (19·2 g., 1·5 mol.) and stearic acid (20·6 g., 1 mol.) were added to a solution of methoxide (from 0·9 g. of sodium and 800 c.c. of methanol), and the mixture electrolysed in a cell fitted with a reflux condenser, a cooling coil (through which water was passed), and two parallel platinum plate cathodes (2 × 3 cm.) placed about 2 mm. on either side of a similar anode. The cell was cooled by immersion in an ice-bath, and a current of about 2·5 amp. was passed until the solution became alkaline (3·5 hr.). It was then neutralised with glacial acid and evaporated. The product was refluxed with ether, the ethereal solution filtered, and the filtrate washed with 5% aqueous potassium hydroxide, then with water, and dried ($MgSO_4$). Distillation gave a

[6] Millin and Polgar, *J.*, 1958, 1902.
[7] Ställberg-Stenhagen and Stenhagen, *Arkiv Kemi, Min., Geol.*, 1947, **24**, *B*, No. 9.
[8] Marks and Polgar, *J.*, 1955, 3851.
[9] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[10] Berner and Leonardsen, *Annalen*, 1939, **538**, 1.
[11] Kenyon and Young, *J.*, 1940, 216.

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fraction, b. p. 158°/10 mm. (5·2 g.), followed by material of b. p. 165°/0·1 mm. (3·6 g.), $[\alpha]_D^{13}$ +1·17° (*c*, 11·12 in ether). The latter was hydrolysed by refluxing it with 10% aqueous-ethanolic (1 : 2) potassium hydroxide for 4 hr. Dilution with water, followed by acidification and ether-extraction, afforded D-(+)-2-*methylheneicosan*-1-*ol*, m. p. 54·5° (from methanol), $[\alpha]_D^{20}$ + 5·49° (*c*, 10·24 in chloroform) (Found: C, 80·5; H, 14·1. $C_{22}H_{46}O$ requires C, 80·9; H, 14·2%).

2(DL) : 4(D)-*Dimethyltricosanoic Acid* (IX).—Toluene-*p*-sulphonyl chloride (4 g.) was added in four portions during 20 min. to a solution of the above alcohol (4·7 g.) in dry pyridine (28 c.c.) at 0°, the mixture being shaken. After a further 6 hr. at 0° with shaking, the mixture was set aside in a refrigerator. Next day it was poured into water, and the precipitate filtered off, then taken up in hot methanol. Cooling gave the *toluene*-p-*sulphonate*, m. p. 43° (Found: C, 72·3; H, 10·8. $C_{29}H_{52}O_3S$ requires C, 72·4; H, 10·9%). This ester was refluxed with a solution of anhydrous sodium iodide (3·6 g.) in dry acetone (35 c.c.) for 24 hr. After dilution with water, the product was extracted with ether, and the extract washed with aqueous sodium thiosulphate and then with water, dried (Na_2SO_4), and evaporated. The resulting crude iodide was refluxed with ethyl sodiomethylmalonate (from 3·2 g. of ethyl methylmalonate, 0·3 g. of sodium, and 10 c.c. of ethanol) for 6·5 hr. After acidification (acetic acid) and dilution with water, the product was isolated by means of ether, then refluxed with a solution of potassium hydroxide (8 g.) in aqueous ethanol (1 : 2; 20 c.c.) for 8·5 hr. The resulting solution was diluted with water and acidified with sulphuric acid, and the product, isolated by ether-extraction, was decarboxylated at 170° (bath) for 1·5 hr., then distilled. The resulting acid (1·7 g.), b. p. 180° (bath)/0·05 mm., was esterified with ethereal diazomethane, and the methyl ester chromatographed in petrol on alumina (100 g.; 30 × 2 cm.) prepared in petrol. The following fractions were taken ($[\alpha]_D$ refers to *c* 5—14 in chloroform at 19°): (1) petrol (100 c.c.) (0·21 g.); (2) petrol (150 c.c.) (0·02 g.); and, all in petrol–benzene (9 : 1): (3) (100 c.c.) (0·15 g., $[\alpha]_D$ −1·05°); (4) (50 c.c.) (0·31 g., $[\alpha]_D$ −5·10°) (Found: C, 78·9; H, 13·4. Calc. for $C_{26}H_{52}O_2$: C, 78·8; H, 13·1%); (5) (50 c.c.) (0·2 g., $[\alpha]_D$ +0·94°); (6) (50 c.c.) (0·12 g., $[\alpha]_D$ +2·28°); (7) (50 c.c.) (0·07 g., $[\alpha]_D$ +2·69°); (8) (100 c.c.) (0·1 g., $[\alpha]_D$ +4·37°).

L-(−)-3-*Methylheneicosanoic Acid* (VI; R = H).—Stearic acid (30 g.; m. p. 69·1—69·5°) was electrolysed with *D*-(−)-(methyl hydrogen β-methylglutarate) [4,5] (8 g.; added in several portions during 2 hr.) in methanol (150 c.c.) and light petroleum (b. p. 60—80°; 150 c.c.) in the presence of potassium methoxide (from 0·7 g. of potassium) at about 2 amp. for 3 hr. The mixture was then cooled (0°) and filtered, and the filtrate diluted with water. The organic layer was separated, and the aqueous layer extracted with ether. The combined extracts were washed with 5% aqueous potassium carbonate and water, dried ($MgSO_4$), and distilled, to give, after a forerun, an ester fraction of b. p. 150—154°/0·04 mm. (4·6 g.). Hydrolysis of the latter with ethanolic potassium hydroxide gave L-(−)-3-*methylheneicosanoic acid* which crystallised from acetic acid as plates, m. p. 56·9°, $[\alpha]_D^{10}$ −3·8° (*c*, 3·0 in chloroform) (Found: C, 77·5; H, 12·9. $C_{22}H_{44}O_2$ requires C, 77·6; H, 12·9%). Its *amide* crystallised from ethanol as needles, m. p. 92° (Found: N, 3·9. $C_{22}H_{45}ON$ requires N, 4·1%).

2(DL) : 4(L)-*Dimethyldocosanoic Acid* (VII).—Reaction of silver *L*-(−)-3-methylheneicosanoate (obtained from the acid *via* the potassium salt, and dried over phosphoric oxide at 100°) with bromine in ethyl bromide by Rottenberg's procedure,[12] followed by condensation of the resulting bromide with ethyl sodiomethylmalonate as described previously for the synthesis of (±)-2 : 4-dimethyldocosanoic acid [13] gave the 2(*DL*) : 4(*L*)-form of the latter. This acid crystallised from petrol as plates, m. p. 54·7°; its *p*-bromophenacyl ester crystallised from ethanol as needles, m. p. 74° (Found: C, 67·6; H, 9·25. Calc. for $C_{32}H_{53}O_3Br$: C, 68·0; H, 9·4%).

We thank Dr. A. G. Long and Mr. J. S. Hunt, of Glaxo Laboratories Ltd., and that Company for the supply of (+)-5-acetoxy-4-methylpentanoic acid.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, September 29th,* 1958.]

[12] Rottenberg, *Helv. Chim. Acta*, 1952, **35**, 1286.
[13] Bailey, Polgar, and Robinson, *J.*, 1953, 3031.

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132. *Intermediates for the Synthesis of Optically Active Methyl-substituted Long-chain Acids. Part V.**

By R. Brettle and N. Polgar.

β-Methoxy-α-methylpropionic acid (V) has been resolved, with isolation of the (+)-enantiomer which is shown to have *L*-configuration.† This enantiomer was converted into the (+)-form of the methoxy-chloride (III; X = Cl); the latter has the requisite configuration for a projected [1] synthesis of mycoceranic acid.

The present work was undertaken in connection with studies in the synthesis of mycoceranic acid. This acid has been shown [2] to have the structure (I) where *n* was stated to be probably 21; all three asymmetric centres were assigned to the *D*-series.[1] From mass-spectrometric studies Asselineau, Ryhage, and Stenhagen [3] concluded that *n* is 22. One of the routes considered earlier [1] for the synthesis of this acid involved a Grignard reaction between the *D*-form of the ketone (II) and the requisite enantiomer of the methoxy-halide (III; X = halogen), to give by further steps the methoxy-derivative (IV). The present paper records the synthesis of the (+)-enantiomer of 1-chloro-3-methoxy-2-methylpropane (III; X = Cl) which is found to be the requisite enantiomer for the above synthesis.

(I) $Me\cdot[CH_2]_n\cdot CHMe\cdot CH_2\cdot CHMe\cdot CH_2\cdot CHMe\cdot CO_2H$

(II) $Me\cdot[CH_2]_n\cdot CHMe\cdot CH_2\cdot COMe$

(III) $X\cdot CH_2\cdot CHMe\cdot CH_2\cdot OMe$ $\qquad$ $MeO\cdot CH_2\cdot CHMe\cdot CO_2H$ (V)

(IV) $Me\cdot[CH_2]_n\cdot \overset{D}{C}HMe\cdot CH_2\cdot \overset{DL}{C}HMe\cdot CH_2\cdot \overset{D}{C}HMe\cdot CH_2\cdot OMe$

The starting point was methyl α-methylacrylate which, by reaction with methanol in the presence of sodium methoxide,[4,5] followed by hydrolysis of the resulting methoxy-ester, gave β-methoxy-α-methylpropionic acid (V). Resolution of this acid was accomplished with quinine, affording the (+)-enantiomer, $[\alpha]_D$ +14·4°, whose configuration was established by the following experiments.

L-(+)-2-Methylpent-4-enoic acid [6] (VI) was converted by way of the corresponding alcohol [7] (VII; R = H) into the methoxy-derivative (VII; R = Me) which on oxidation with sodium metaperiodate and potassium permanganate (cf. Lemieux and von Rudloff [8]) afforded *D*-(−)-γ-methoxy-β-methylbutyric acid (VIII) (the change of prefix *L* to *D* is due to the conventional † alteration of the reference group).

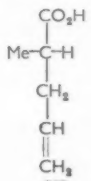
A lævorotatory specimen of γ-methoxy-β-methylbutyric acid also resulted from a partially resolved sample of the (−)-enantiomer of β-methoxy-α-methylpropionic acid (V) by reduction to the corresponding alcohol (III; X = OH) and conversion of the latter through the iodide (III; X = I) into the cyanide (III; X = CN), followed by hydrolysis (*i.e.*, by a sequence of reactions involving no change of configuration). It follows that the (−)-enantiomer of the methoxy-acid (V) has *D*-configuration; consequently, the above fully resolved (+)-form of this methoxy-acid is the *L*-isomer.

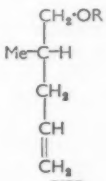
* Part IV, *J.*, preceding paper.

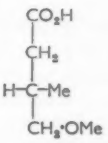
† The symbols *D* and *L* are used in the sense defined by Linstead, Lunt, and Weedon (*J.*, 1950, 3333).

[1] Marks and Polgar, *J.*, 1955, 3851.
[2] Polgar, *J.*, 1954, 1011.
[3] Asselineau, Ryhage, and Stenhagen, *Acta Chem. Scand.*, 1957, **11**, 96.
[4] Bieber, *Compt. rend.*, 1952, **234**, 1783.
[5] Bieber, *Ann. Chim. France*, 1954, **9**, 674.
[6] Ställberg-Stenhagen, *Arkiv Kemi, Mineralog. Geol.*, 1946, **23**, *A*, No. 15.
[7] Fray and Polgar, *J.*, 1956, 2036.
[8] Lemieux and von Rudloff, *Canad. J. Chem.*, 1955, **33**, 1701, 1710.

Reduction of the *L*-(+)-enantiomer of the methoxy-acid (V) with lithium aluminium hydride gave (−)-3-methoxy-2-methylpropan-1-ol (III; X = OH) which on reaction with thionyl chloride in the presence of pyridine afforded (+)-1-chloro-3-methoxy-2-methylpropane (III; X = Cl). A Grignard reaction between this chloride and the *D*-form of the ketone (II), followed by the stages already mentioned,[1] would give the methoxy-derivative (IV) in the requisite 2(*D*) : 6(*D*)-form, the change in prefix in respect of the asymmetric centre at $C_{(2)}$ [corresponding to the active centre in the *L*-enantiomer of the methoxy-acid (V)] following from the conventional alteration of the reference group.


(VI)


(VII)


(VIII)

It is of interest that *D*-γ-methoxy-β-methylbutyric acid (VIII) is, as shown above, lævorotatory, whereas *D*-6-methoxy-3-methylhexanoic acid was dextrorotatory.[9] The sign of rotation of these methoxy-acids is in agreement with earlier findings[10] that all 3(*D*)-methylalkanoic acids $Me\cdot[CH_2]_n\cdot CHMe\cdot CH_2\cdot CO_2H$ are dextrorotatory with the exception of the first member of this series ($n = 1$).

Experimental

α refers to homogeneous liquids ($l = 1$). Ethereal solutions were dried over Na_2SO_4.

β-Methoxy-α-methylpropionic Acid (V).—Methyl β-methoxy-α-methylpropionate, b. p. 148—149°, was obtained in 43% yield by Bieber's procedure [5] (Bieber [5] gives the same b. p.; Glover and Jones [11] referring to Bieber's note,[4] but unaware of his later paper,[5] report yields varying from 0 to 30%). Hydrolysis of this ester according to Bieber's directions [5] gave β-methoxy-α-methylpropionic acid, b. p. 114°/24 mm., which formed a *p*-bromophenacyl ester of m. p. 63·5° (from aqueous ethanol) (Bieber [5] gives m. p. 63·5—64°; Gresham [12] records b. p. 110—112°/20 mm. for the acid).

Resolution of β-Methoxy-α-methylpropionic Acid.—The (±)-acid (60 g., 1 mol.) and quinine (164·6 g., 1 mol.) were dissolved in hot acetone (1·5 l.) and the mixture set aside. The quinine salt which crystallised overnight gave, after three recrystallisations from acetone, on decomposition with 2N-hydrochloric acid followed by ether-extraction and distillation, an acid with α_D^{22} +12·4°. After three further recrystallisations of the quinine salt the regained acid had α_D^{22} +14·64°; a further recrystallisation of the quinine salt gave acid with the same rotation. In further experiments six batches (in all 367 g.) of the racemic acid were resolved by this procedure. The (+)-*acid* so obtained had $\alpha_D^{17\cdot5}$ +15·02° and α_D^{19} +14·98° (for two different specimens), d_{19}^{19} 1·04, $[\alpha]_D^{19}$ +14·4° (Found: C, 50·8; H, 8·4; OMe, 25·8. $C_5H_{10}O_3$ requires C, 50·8; H, 8·4; OMe, 26·3%).

The mother-liquors from the first crystallisation of the quinine salt yielded acid having α_D^{21} −8·14°.

In other experiments the partially resolved (+)-acid was obtained by resolution with cinchonidine. After eight recrystallisations of the cinchonidine salt from acetone the regained acid had α_D^{24} +13·08°; the mother-liquors of the first crystallisation of the cinchonidine salt (from acetone) gave acid having α_D^{20} −4·74°.

3-Methoxy-2-methylpropan-1-ol (III; X = OH).—The above fully resolved (+)-acid (19 g.) in ether (100 c.c.) was added to a stirred mixture of lithium aluminium hydride (9·2 g.) and ether (150 c.c.) during 2 hr., at such a rate that the ether boiled gently. After a further 0·5 hr.

[9] Brettle and Polgar, *J.*, 1956, 1620.
[10] Mills and Klyne, in "Progress in Stereochemistry," Butterworths, London, 1954, Vol. I, p. 205.
[11] Glover and Jones, *J.*, 1958, 3021.
[12] Gresham, U.S.P. 2,504,080 (see *Chem. Abs.*, 1950, **44**, 6878).

XUM

the excess of lithium aluminium hydride was decomposed in the usual manner; concentrated hydrochloric acid (90 c.c.) was then added, and stirring continued for another 0·5 hr. The ethereal layer was separated, and the aqueous phase extracted with ether (continuous extractor). The combined ethereal solutions were shaken with potassium carbonate, dried, and distilled, affording (−)-3-*methoxy*-2-*methylpropan*-1-*ol* (12·65 g.), b. p. 154—156°, n_D^{21} 1·4160, α_D^{23} −2·26°, d_{23}^{23} 0·915, $[\alpha]_D^{23}$ −2·47°. Elderfield, Pitt, and Wempen [13] record b. p. 154—155°, n_D^{27} 1·4140, d^{27} 0·916, for the racemic alcohol.

The partially resolved (−)-enantiomer of β-methoxy-α-methylpropionic acid (24·7 g.) having α_D^{21} −8·14° (see above) gave by the foregoing procedure partially active alcohol (16·63 g.) with α_D^{23} +1·14°.

The (±)-acid gave, by the same procedure, (±)-3-methoxy-2-methylpropan-1-ol, b. p. 154—156°, yielding a 3 : 5-dinitrobenzoate as needles of m. p. 63·5° (from aqueous ethanol or light petroleum, b. p. 60—80°) (Found: OMe, 10·3; N, 9·5. Calc. for $C_{12}H_{14}O_7N_2$: OMe, 10·4; N, 9·4%). Elderfield *et al.*[13] record m. p. 63—64°.

(+)-1-*Chloro*-3-*methoxy*-2-*methylpropane* (III; X = Cl).—This was obtained from (−)-3-methoxy-2-methylpropan-1-ol by means of thionyl chloride in the presence of pyridine according to the directions given by Elderfield *et al.*[13] for the racemic chloride. The (+)-*chloride* had b. p. 125°, α_D^{24} +12·68°, d_{20}^{24} 0·963, $[\alpha]_D^{24}$ +13·2°. Elderfield *et al.*[13] record b. p. 124—124·5°, d_4^{27} 0·966, for the racemic chloride.

5-*Methoxy*-4-*methylpent*-1-*ene*.—2-Methylpent-4-en-1-ol [7·2 g.; obtained from (±)-2-methylpent-4-enoic acid by the procedure described [7] for the preparation of the (−)-enantiomer] was refluxed with methyl iodide (30·5 g.) and silver oxide (25 g.; prepared according to the directions of Helferich and Klein; [14] added in 5 g. portions) for 7 hr. The mixture was filtered, and the silver salts were washed with ether; the filtrate and washings were then evaporated. After two further methylations by the same procedure, the product was distilled, affording 5-*methoxy*-4-*methylpent*-1-*ene* (1·65 g.), b. p. 109° (Found: C, 73·7; H, 12·4. $C_7H_{14}O$ requires C, 73·7; H, 12·3%).

D-(−)-γ-*Methoxy*-β-*methylbutyric Acid* (VIII).—(i) *L*-(−)-2-Methylpent-4-en-1-ol (VII; R = H) [12·6 g.; obtained from *L*-(+)-2-methylpent-4-enoic acid [6] by the procedure described earlier [7]] was converted into the methoxy-derivative (VII; R = Me) according to the directions given above for the racemic product, except that the methylation procedure was repeated three times, and the silver salts were exhaustively extracted with boiling chloroform. Distillation of the product gave a fraction (7·9 g.), b. p. 90—115°, which on redistillation yielded the methoxy-derivative (4·35 g.), b. p. 108—112°. 0·64 g. of this product was oxidised with sodium metaperiodate (1·58 g.) and potassium permanganate (212 mg.) in aqueous sodium carbonate by the procedure of Lemieux and von Rudloff.[8] The mixture was kept at room temperature for 21 hr. with occasional shaking, then acidified with 2N-sulphuric acid and extracted with ether (continuous extractor). Six further batches (in all 4·1 g.) were oxidised by this procedure. The combined ethereal extracts gave on distillation D-(−)-γ-*methoxy*-β-*methylbutyric acid* (1·37 g.), b. p. 124—128°/20 mm., n_D^{18} 1·4258, $[\alpha]_D^{22}$ −8·7° (*c* 17·8 in Et_2O, *l* 0·5) (Found: C, 54·1; H, 9·4. $C_6H_{12}O_3$ requires C, 54·5; H, 9·1%). Wagner [15] gives b. p. 123—125°/20 mm., n_D^{20} 1·4235, for the racemic acid. The S-*benzylthiuronium salt* had m. p. 141·5° after crystallisation from water (Found: S, 10·8; N, 9·8. $C_{14}H_{22}O_3N_2S$ requires S, 10·7; N, 9·4%).

(ii) A partially active sample of *D*-(−)-γ-methoxy-β-methylbutyric acid was obtained from partially resolved (+)-3-methoxy-2-methylpropan-1-ol (see above), α_D^{23} 1·14°, by the following procedure.

Dry pyridine (24·9 g., 2·1 mol.) was gradually added with stirring to an ice-cold mixture of the (+)-alcohol (15·6 g., 1 mol.) and toluene-*p*-sulphonyl chloride (30 g., 1·05 mol.) during about 2 hr. The product was acidified with dilute hydrochloric acid, then extracted with ether, and the dried (K_2CO_3) extract was evaporated. The resulting crude toluene-*p*-sulphonate was refluxed with a solution of anhydrous sodium iodide (41 g.) in dry acetone (450 c.c.), with stirring, for 7 hr. The iodide, isolated in the known manner, was added during 15 min. in ethanol (150 c.c.) to a hot solution of potassium cyanide (11·85 g.) in water (40 c.c.), and the solution heated under reflux for 16½ hr. The resulting crude cyanide, isolated by ether-extraction, was refluxed with a mixture of concentrated sulphuric acid (40 c.c.), acetic acid (40 c.c.),

[13] Elderfield, Pitt, and Wempen, *J. Amer. Chem. Soc.*, 1950, **72**, 1334.
[14] Helferich and Klein, *Annalen*, 1926, **450**, 219.
[15] Wagner, *J. Amer. Chem. Soc.*, 1949, **71**, 3214.

and water (80 c.c.) for 8 hr. The product was poured into water and extracted with ether from which the acidic fraction was removed with aqueous sodium hydrogen carbonate. Acidification of the alkaline extract and ether-extraction, followed by distillation, gave (−)-acid (3·85 g.), b. p. 127°/25 mm., n_D^{16} 1·4270, $[\alpha]_D^{23}$ −5·7° (*c* 15 in Et_2O; *l* 0·5) (Found: C, 54·5; H, 9·2%).

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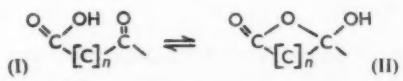
133. *Infrared Spectra and Dehydrogenase Activity of Isatin Derivatives.*

By P. W. SADLER, H. MIX, and H. W. KRAUSE.

The vibrational spectra of 7-methylisatin-4-carboxylic acid and related compounds have been examined. The lactol form of the acid is present in the solid state; normal carboxylic acid dimerisation occurs in concentrated solution, and an intramolecularly bonded form exists in dilute solution. Various hydrogen-bonded forms occur in the derivatives, and the possible relation between these structures and the dehydrogenase activity is discussed.

EARLIER publications [1,2] have related dehydrogenase activities of substituted isatins to the stretching frequencies of the carbonyl groups. This work has now been extended by an analysis of the spectra of the highly active 7-methylisatin-4-carboxylic acid and its derivatives.[3] The variety of structures which may be written for the acid include the keto–lactol tautomers and two hydrogen-bonded forms involving the carboxyl group. Numerous examples of keto–lactol tautomerism have been described in the literature, many of them occurring in γ-ketonic acids (I; $n = 2$). Various of these compounds have been shown to be biologically active, such as *o*-benzoylbenzoic acid,[4] and the weakly antibacterial mould products, penicillic [5,6] and gladiolic acid.[7] Such compounds may usually be recognised by the formation of two series of esters, the normal carboxylic esters and the



(I) (II)

hydroxy-lactonic esters derived from (I) and (II) respectively, although benzil-*o*-carboxylic acid forms only the normal methyl ester. Ultraviolet absorption spectra have been extensively used in the elucidation of the structures of γ-ketonic acids,[8] and more recently infrared spectroscopy has been used.[9] For isatincarboxylic acids, the interpretation of infrared data is difficult because the carbonyl stretching frequency of the carboxyl group overlies, and in some cases merges with, the α- and the β-carbonyl frequency, but the use of several reference compounds has made band assignment reasonably certain. The compounds under investigation are insoluble in non-polar solvents such as carbon disulphide and carbon tetrachloride, and in weakly polar solvents such as chloroform, but are soluble in dimethylformamide and dioxan which, unfortunately, are not satisfactory. However, a suitable compromise was found in the use of *sym*-tetrachloroethane.

[1] O'Sullivan and Sadler, *J.*, 1956, 2202.
[2] *Idem, Arch. Biochem. Biophys.*, 1957, **65**, 243.
[3] Mix and Krause, *Chem. Ber.*, 1956, **89**, 2630.
[4] Sexton and Templeman, *Nature*, 1948, **161**, 974.
[5] Birkinshaw, Oxford, and Raistrick, *Biochem. J.*, 1936, **30**, 394.
[6] Raphael, *Nature*, 1947, **160**, 261.
[7] Brian, Curtis, Grove, Hemming, and McGowan, *ibid.*, 1946, **157**, 697.
[8] Shaw, *J. Amer. Chem. Soc.*, 1946, **68**, 2510.
[9] Grove and Willis, *J.*, 1951, 877.

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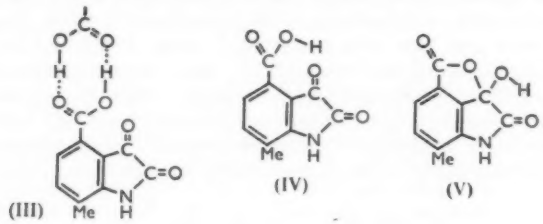
Typically, the infrared spectra of substituted isatins in chloroform and tetrachloroethane possess a broad band between 3500 and 3200 cm.$^{-1}$, which contains two maxima, a fairly sharp peak (see Table 1) at about 3450 cm.$^{-1}$ and a broader maximum near 3230 cm.$^{-1}$; the former is an N–H stretching frequency and the latter results from the intermolecular NH · · · O=C bonding, which exists in all but a few ring-substituted isatins.[1] Two carbonyl maxima normally occur near 1740 and 1755 cm.$^{-1}$; the absorption of the lower frequency is attributed to the β-carbonyl group and is sharp and intense, whilst the α-carbonyl absorption is always slightly less intense and, although usually present as a well-defined maximum, is occasionally evident only as a shoulder.[1] In general, the separation of the two carbonyl peaks is less distinct in 4- and 6-substituted compounds, the resonance structures presumably tending to equalise the character of the two carbonyl groups. These compounds are the least soluble in solvents of low polarity and from the character of the 3230 cm.$^{-1}$ absorption appear to possess very strong intermolecular links.[1] A 1620 cm.$^{-1}$ band is present which is always comparable in intensity with the carbonyl frequencies and in a few cases is divided into two high peaks with maxima respectively slightly above and below 1620 cm.$^{-1}$. Some compounds possessing 4-substituents show a maximum at a slightly lower frequency, in accordance with the usual behaviour of vicinally substituted benzene derivatives.

7-Methylisatin-4-carboxylic acid (III) in concentrated solution in *sym*-tetrachloroethane shows only the broad bonded O–H absorption at 2800—3200 cm.$^{-1}$, characteristic of the carboxylic acid dimer superimposed on the C–H stretching absorption at 2850 cm.$^{-1}$; the NH peaks are not clearly defined. The α- and the β-carbonyl stretching frequency



occur at 1760 and 1735 cm.$^{-1}$ respectively, both being very weak in comparison with the intense absorption at 1670 cm.$^{-1}$. This is slightly lower than the typical aromatic carboxylic acid dimer band at 1685 cm.$^{-1}$ and is in agreement with Flett's findings [10] that aromatic acids which are capable of internal hydrogen-bonding have the dimer band below 1680 cm.$^{-1}$. The band at 1590 cm.$^{-1}$ is an aromatic frequency. On dilution, the 1670 cm.$^{-1}$ peak steadily diminishes and a new intense peak appears at 1705 cm.$^{-1}$ due to the monomeric form (IV), which is intramolecularly bonded as no absorption at 3600 cm.$^{-1}$ characteristic of free OH groups is shown. The β-carbonyl peak no longer occurs as a separate entity, but weak absorption is still shown at 1760 cm.$^{-1}$. The amide corresponding to this acid shows typical free and bonded N–H stretching frequencies at 3500 and 3340 cm.$^{-1}$ respectively. The C–H stretching frequency occurs as a well-defined maximum at 2900 cm.$^{-1}$ and the α- and the β-carbonyl group give rise to a fairly broad band at 1735 cm.$^{-1}$. The amide I band occurs as a strong peak at 1710 cm.$^{-1}$. Associated and unassociated forms may give rise to two amide II bands,[11] which appear as two split maxima at 1641—1566. The aromatic frequency bands appear at 1560 and 1615 cm.$^{-1}$.[12] The situation is similar in the case of the propylamide, except that the N–H absorption closely approximates to that of isatin itself; presumably the amide N–H is bonded to the β-carbonyl group, the stretching frequency of which could be masked by the strong amide I band at 1720 cm.$^{-1}$;

[10] Flett, *J.*, 1951, 962.
[11] Richards and Thompson, *J.*, 1947, 1248.
[12] Bomstein, *Analyt. Chem.*, 1953, **25**, 512.

alternatively, the α- and the β-carbonyl stretching frequency may form a single band at 1762 cm.$^{-1}$. The amide II band is clearly defined as a single maximum at 1650 cm.$^{-1}$, the aromatic frequencies appearing at 1620 and 1580 cm.$^{-1}$. The dipropylamide, in accord with other *NN*-disubstituted amides, has no amide II band; again the amide I band at 1735 cm.$^{-1}$ may have the β-carbonyl stretching frequency superimposed, or both isatin carbonyl groups may give rise to the single band at 1755 cm.$^{-1}$.

5-Carboxymethylisatin was chosen as a reference compound as it is isomeric with 7-methylisatin-4-carboxylic acid but may form only intermolecular hydrogen-bonds. As this compound is a substituted phenylacetic acid its spectrum bears a closer relation to that of a saturated carboxylic acid than to that of an aromatic acid.[10] The strong absorption at 1708 cm.$^{-1}$ is typical of the dimeric form. The absence of free OH absorption confirms this, the bonded OH of the carboxylic acid dimer giving rise to the typical broad band with a weak maximum at 2850 cm.$^{-1}$ where it is superimposed on the C–H stretching frequency. At the concentration used, which was the limit of solubility of this compound, the carbonyl frequencies did not appear as separate entities, but a saturated solution of the more soluble methylated derivative, 5-carboxymethyl-1-methylisatin, showed strong carbonyl absorption at 1735 cm.$^{-1}$, of equal intensity to that of the 1708 cm.$^{-1}$ dimer band. 1-Methylisatin also possesses a single carbonyl peak.[1] The bonded OH absorption of 5-carboxymethyl-1-methylisatin was similar to that observed with the unmethylated 5-carboxymethylisatin. The last two compounds in Table 1, the ethyl esters, were included

TABLE 1. *Infrared spectra of substituted isatins in* sym*-tetrachloroethane.*

Substituent										
None [a]	—	1619	—	—	—	1736	1755sh	2920	3230	3420
4-CO_2H-7-Me [a]	1590	—	—	1670w	1705s	—	1760w	—	—	—
4-CO_2H-7-Me [b]	1590	—	—	1670s	—	1735w	1760sh	2850	(2800—3200)	
4-CO·NH_2-7-Me [a]	1560	1615	1641—1655	—	1710s	1735	—	2900	3340	3500
4-CO·NHPr-7-Me [a]	1580	1620	1650	—	1720	—	1762	2920	3300	3425
4-CO·NPr_2-7-Me [a]	1595	1625	—	—	—	1735	1755	2920	—	3425
5-CH_2·CO_2H [a]	—	1625w	—	—	1708s	—	—	—	—	—
5-CH_2·CO_2H-1-Me [a]	—	1625	—	—	1708	—	—	—	—	—
" [b]	1600	1625	—	—	1708	1735br	—	—	—	—
5-CH_2·CO_2Et-1-Me [a]	—	1625w	—	—	1710	—	—	2920	—	—
5-CH_2·CO_2Et [a]	—	1625w	—	—	1710	—	—	2920	3230	3420

[a] 10^{-3}M-Solution in 0·35 mm. cell. [b] Saturated soln. in 0·35 mm. cell. w = weak, s = strong, br = broad, sh = shoulder.

to show that overtones were not responsible for the absorption in the bonded OH region; the bonded and free NH stretching frequencies of the last compound were similar to those of isatin; no significant absorption was detected in the 3 μ region for the penultimate compound.

The infrared spectral data obtained from the compounds in potassium bromide discs are presented in Table 2. The relation to the spectra obtained from solutions is quite

TABLE 2. *Infrared spectra of substituted isatins (potassium bromide discs).*

Substituents									
None	—	1615	—	—	1730	2900	3200	—	3420
4-CO_2H-7-Me	1595	1620	—	1700w	1740s	2900	3150	—	3400
4-CO·NH_2-7-Me	1560	1624	1650	1698	1728	2850	3190	3300	3400
4-CO·NHPr-7-Me	1580	1615	1630	1710	1755	2900	3190	—	3400
4-CO·NPr_2-7-Me	1590	1628	—	—	1745	2900	3200	—	3400
5-CH_2·CO_2H	—	1621	—	—	1730		2800—3200		
5-CH_2·CO_2H-1-Me	1605	1625	—	1721	1740		2800—3200		
5-CH_2·CO_2Et-1-Me	—	1625	—	1715	1735/1748	—	—	—	—
5-CH_2·CO_2Et	—	1623	—	1723	1738/1745	2900	3200	—	3420

XUM

clear, and band assignments are similar, but the small frequency fluctuations which are always associated with solid-state spectra are present. The variability of the spectra of substituted benzoic acids in alkali halide discs has been discussed by Farmer,[13] but with the particular preparative conditions used the 7-methylisatin-4-carboxylic acid disc should exhibit the dimer band. This band is, however, absent and a new intense peak appears at 1740 $cm.^{-1}$. As a similar band has been described for the lactol form of benzil-*o*-carboxylic acid,[9] it is possible that the lactol form (V) of 7-methylisatin-4-carboxylic acid is the preferred configuration in the solid state, rather than the dimer (III).

It is not possible, in the case of 7-methylisatin-4-carboxylic acid, to relate dehydrogenase activity to the carbonyl stretching frequencies as the latter do not occur as discrete entities. Nor may the high catalytic activity [5] be compared with the σ values for the substituents as the carboxyl group is *ortho* to the β-carbonyl group. However, attention has already been drawn to the possible relation between the unusual dehydrogenase activity of isatins substituted with acid groups in the 4-position and *intra*molecularly hydrogen-bonded structures which may occur in these compounds.[14] This is supported by our results, as under conditions approximating to those used in the measurements of catalytic activity, 7-methylisatin-4-carboxylic acid is shown to exist predominantly in an *intra*molecularly hydrogen-bonded form. But there is obviously no simple relation between bonding propensity and the dehydrogenase activity of 4-substituted isatins, as both the simple amide and the propylamide possess *intra*molecular hydrogen-bonds, yet there is considerable discrepancy between their relative dehydrogenase activities (see

TABLE 3. *Times required for the decolorisation of Methylene Blue in the oxidation of alanine.*

Catalyst: Isatin	Concn. (10^{-5}M)	Time (min.)	Catalyst: Isatin	Concn. (10^{-5}M)	Time (min.)
Unsubst.	2	59	4-CO·NPr_2-7-Me ...	2	**353**
4-CO_2H-7-Me	2	4·5	4-CO·NH_2-7-Me ...	2	Not decolorised
4-CO·NHPr-7-Me	2	50	4-CO·NH_2-7-Me ...	5×10^{-5}	1,002

Table 3). The very low activity of the unsubstituted amide is difficult to explain. No spectral evidence has been obtained to support the suggestion that in this case a stable intermediate is formed between the substituted isatin and the amino-acid involved in the dehydrogenation, although this would provide a simple explanation of the phenomenon. Generally, the interpretation of *ortho*-substituent effects is complex, and a more extensive investigation will be required if the anomalous results for these 4-substituted isatins are to be fully explained.

Experimental.—Spectra were determined by using a Perkin-Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism.

COURTAULD INSTITUTE OF BIOCHEMISTRY, MIDDLESEX HOSPITAL, MEDICAL SCHOOL, LONDON, W.1.
INSTITUT FÜR KATALYSEFORSCHUNG, ROSTOCK, DER DEUTSCHEN AKADEMIE DER WISSENSCHAFTEN ZU BERLIN. [*Received, October 7th*, 1958.]

[13] Farmer, *Spectrochim. Acta*, 1956, **8**, 374.
[14] Mix, Krause, and Reihsig, *J. prakt. Chem.*, 1958, **6**, 174.

134. *Synthesis of Diterpenes. Part II.* An Intermediate for the Synthesis of Diterpenoid Acids.*

By J. A. Barltrop and A. C. Day.

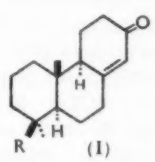
Cyclisation with phosphoric oxide (but not with polyphosphoric acid) of the tertiary alcohol (II) gives the *cis*- and *trans*-octahydrophenanthrenecarboxylic esters (VI; R = CO_2Et) and (V; E = Et) respectively. The latter is converted into the tricyclic (±)-keto-ester (I; R = CO_2Me), identical with a degradative product of agathenedicarboxylic acid.

Work on the synthesis of the diterpenoid resin acids has so far concerned those which contain an aromatic ring,[1] and has culminated in the total syntheses of podocarpic acid by King, King, and Topliss [2] and of dehydroabietic acid by Stork and Schulenberg.[3] Difficulties would be expected to be greater with non-aromatic resin acids, *e.g.*, abietic and agathenedicarboxylic acids, where the number of asymmetric centres is greater.

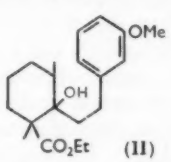
A possible approach to such acids is offered by the tricyclic keto-esters (I; R = CO_2Me) and (VIII) which were obtained by degradation of agathenedicarboxylic acid [4] and *neo*-abietic acid [5] respectively; and a route analogous to that to the ketone [6] (I; R = Me) has now led to one of these intermediates (I; R = CO_2Me).

Condensing ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate with the Grignard reagent from *m*-methoxyphenylacetylene in tetrahydrofuran gave a 57% yield of ethyl 2-hydroxy-2-*m*-methoxyphenylethynyl-1 : 3-dimethyl*cyclo*hexanecarboxylate, the triple bond of which was almost quantitatively reduced over palladized charcoal to give the 2-*m*-methoxyphenethyl-alcohol (II).

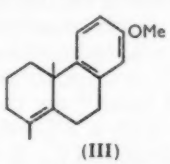
Cyclization of this compound was first tried with polyphosphoric acid (cf. refs. 2 and 6), but loss of the elements of ethanol and carbon monoxide occurred, giving a material whose analyses indicated a hexahydro-7-methoxy-1 : 12-dimethylphenanthrene but which was probably a mixture of double-bond isomers. On hydrogenation it absorbed less than 0·5 mol. of hydrogen, suggesting that the isomer (III) with a tetrasubstituted double bond predominated. The unsaturated ester (IV) also lost ethanol and carbon monoxide when



(I)



(II)



(III)

cyclized under these conditions. However, treatment of the hydroxy-ester (II) with phosphoric oxide at 140—145° (cf. ref. 7) gave a mixture from which two stereoisomeric, tricyclic esters, A (V; R = Et) (25%) and B (VI; R = CO_2Et) (21%), were isolated by chromatography. Each ester was shown to be stereochemically homogeneous by the infrared spectra of fractions collected during chromatography. Minor products were the unsaturated ester (IV) (2%) and the mixture of hexahydro-7-methoxy-1 : 12-dimethylphenanthrenes (14%). The unsaturated ester (IV) gave a similar mixture when treated with phosphoric oxide.

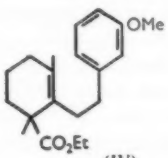
* Part I, *J.*, 1958, 2566.

[1] Haworth and Barker, *J.*, 1939, 1299; Bhattacharyya, *J. Indian Chem. Soc.*, 1945, **22**, 165; Haworth and Moore, *J.*, 1946, 633; Parham, Wheeler, and Dodson, *J. Amer. Chem. Soc.*, 1955, **77**, 1166; Saha, Ganguly, and Dutta, *Chem. and Ind.*, 1956, 412.
[2] King, King, and Topliss, *ibid.*, p. 113.
[3] Stork and Schulenberg, *J. Amer. Chem. Soc.*, 1956, **78**, 250.
[4] Ruzicka, Bernold, and Tallichet, *Helv. Chim. Acta*, 1941, **24**, 223.
[5] Harris and Sanderson, *J. Amer. Chem. Soc.*, 1948, **70**, 339.
[6] Barltrop and Rogers, *Chem. and Ind.*, 1957, 20; *J.*, 1958, 2566.
[7] King, King, and Topliss, *Chem. and Ind.*, 1954, 108; *J.*, 1957, 573.

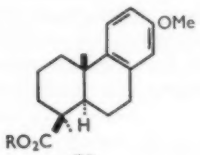
XUM

Esters A and B, and methyl *O*-methylpodocarpate, which are all esters of tricyclic, tertiary acids, were shown by infrared spectroscopy to lose the ethoxycarbonyl group when treated with polyphosphoric acid. In view of these results, the success of King *et al.*[2] in cyclising the hydroxy-ester (VII) with polyphosphoric acid to a mixture of diastereoisomeric, tricyclic esters (including ethyl *O*-methylpodocarpate) in 88·5% yield is surprising. In the polyphosphoric acid reactions carried out in the present investigation, loss of ethanol and carbon monoxide is presumably preceded by generation of $R{\cdot}CO^+$ from the protonated ester group:[8] the retention of the ethoxycarbonyl group in the phosphoric oxide cyclization can then be understood in terms of steric factors which make interaction between this group and the Lewis acid difficult.

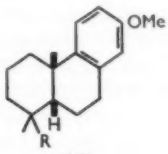
Hydrolysis of the esters A (V; R = Et) and B (VI; R = CO_2Et) was very difficult; but comparative experiments showed that ester A contains an ester group appreciably more hindered than that of ester B. Thus, when heated with a 30% solution of potassium hydroxide in slightly aqueous ethylene glycol at 150° for 5 hr., esters A and B gave 35 and 87% yields, respectively, of the corresponding acids. Both acids gave methyl esters when treated with diazomethane.



(IV)



(V)



(VI)

Reduction of the aromatic ring of esters A and B with lithium, ethanol, and liquid ammonia required very vigorous conditions. Wilds and Nelson's technique[9] reduced the esters to the corresponding primary alcohols (cf. ref. 10), leaving the aromatic ring unchanged: the acids (V; R = H) and (VI; R = CO_2H) were unaffected, and the alcohol (VI; R = $CH_2{\cdot}OH$) and its tetrahydropyranyl ether showed only traces of further reduction when treated with lithium under these conditions. However, by use of "lithium-bronze" and a greater proportion of ethanol,[11] followed by fission of the resulting enol ether with ethanolic hydrochloric acid, ester A was converted into 16-hydroxypodocarp-8-en-7-one (I; R = $CH_2{\cdot}OH$) in 57% yield. [The nomenclature of compounds derived from ester A is based[12] on the hydrocarbon podocarpane (IX).] Oxidation of this hydroxy-ketone with a 2% solution of chromium trioxide in acetic acid gave 7-oxopodocarp-8-en-16-oic acid (I; R = CO_2H). The keto-acid was also obtained by reduction of acid A with "lithium-bronze," followed by treatment with ethanolic hydrochloric acid, but the yield was very poor.

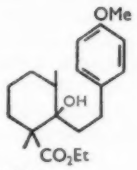
Methyl (±)-7-oxopodocarp-8-en-16-oate (I; R = CO_2Me), m. p. 98—99°, was obtained by treatment of the keto-acid with diazomethane. Its infrared absorption spectrum, determined in carbon disulphide solution, was identical with that of the pure dextrorotatory keto-ester, which had been obtained[4] from agathenedicarboxylic acid. The synthetic and the dextrorotatory keto-ester showed identical conjugated-carbonyl absorptions in the ultraviolet region ($\lambda_{max.}$ 241 mμ, log ε 4·25).

Similarly, reduction of ester B by "lithium-bronze," followed by treatment with acid, gave a hydroxy-ketone (X; R = $CH_2{\cdot}OH$) which was converted by chromic acid into a keto-acid. Esterification with diazomethane gave a keto-ester (X; R = CO_2Me), m. p.

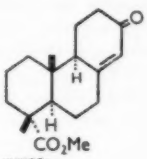
[8] Elliott and Hammick, *J.*, 1951, 3402.
[9] Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360, 5366.
[10] Chablay, *Compt. rend.*, 1913, **156**, 1020; *Ann. Chim.*, 1917, **8**, 213; Kharasch, Sternfeld, and Mayo, *J. Org. Chem.*, 1940, **5**, 362.
[11] Cf. Johnson *et al.*, *J. Amer. Chem. Soc.*, 1956, **78**, 6331, 6339, 6354.
[12] Klyne, *J.*, 1953, 3072.

XUM

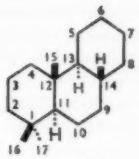
106—107°. That the synthetic keto-ester was not identical with the tricyclic keto-ester (VIII) derived [5] from *neo*abietic acid was shown by comparison of their infrared spectra.



(VII)

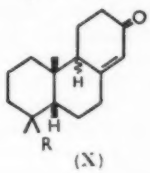


(VIII)

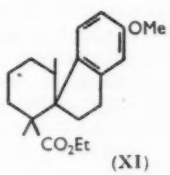


(IX)

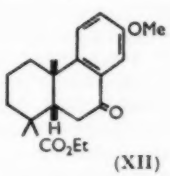
Ester B and the compounds related to it are considered to have a *cis*-AB-ring junction; the possibility that they are spirans, *e.g.*, (XI), is excluded because oxidation of ester B with a 20% solution of chromium trioxide in acetic acid [13] gave a compound which had the infrared absorption characteristic of an α-tetralone (carbonyl band at 1686 cm.$^{-1}$). A spiran structure (XI) for ester B would lead on oxidation to an indan-1-one which would show carbonyl absorption at a higher frequency [14] (1715—1706 cm.$^{-1}$). The oxidation product is therefore formulated as (XII), the stereochemistry at position 1 (phenanthrene numbering) being as yet undefined. The formation of an appreciable amount of acidic material in the chromic acid oxidation of the ester is in accord with Wenkert and Jackson's observations [13] on the oxidative behaviour of 1 : 1-disubstituted *cis*-AB-hydrophenanthrenes related to the diterpene acids.



(X)



(XI)



(XII)

The stereochemistry at position 13 in the hydroxy-ketone (X; R = CH_2·OH) and in the related keto-acid and ester (X; R = CO_2H, and CO_2Me) is uncertain: models fail to reveal any decisive difference between the 13α-H and 13β-H isomers.

A preliminary account of this work has been published.[15]

Experimental

Ultraviolet spectra were measured for ethanol solutions; infrared spectra were determined for liquid films unless otherwise stated. M. p.s were determined on a Kofler block. For chromatography, Peter Spence's "Grade H" alumina was used; deactivated alumina contained 5% of 10% aqueous acetic acid. Unless otherwise stated, "light petroleum" refers to the fraction of b. p. 60—80°.

m-Methoxyphenylacetylene, prepared from *m*-methoxyacetophenone,[16] or much more conveniently [17] from *m*-methoxycinnamic acid, had b. p. 86—88°/12—13 mm., n_D^{16} 1·5581 (lit.,[16] b. p. 85°/13 mm., n_D^{25} 1·5560).

Ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate, prepared by Haworth and Barker's method,[1] had b. p. 117°/16 mm., n_D^{18} 1·4498 (lit.,[18] n_D^{20} 1·4491).

*Ethyl 2-Hydroxy-2-m-methoxyphenylethynyl-1 : 3-dimethyl*cyclo*hexanecarboxylate.*—To a boiling solution of the Grignard reagent prepared from magnesium (7·7 g.) and ethyl bromide (37 g.)

[13] Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.
[14] Gutsche, *ibid.*, 1951, **73**, 786.
[15] Barltrop and Day, *Chem. and Ind.*, 1958, 439.
[16] Johnson, Banerjee, Schneider, Gutsche, Shelberg, and Chinn, *J. Amer. Chem. Soc.*, 1952, **74**, 2843.
[17] Barltrop, Bigley, and Rogers, unpublished work.
[18] Parham, Wheeler, Dodson, and Fenton, *J. Amer. Chem. Soc.*, 1954, **76**, 5380.

in dry ether (100 c.c.) and pure tetrahydrofuran (200 c.c.) under nitrogen, *m*-methoxyphenylacetylene (42 g.) in tetrahydrofuran (80 c.c.) was added during ½ hr. with stirring. Boiling was continued for 1 hr., and then ethyl 1 : 3-dimethyl-2-oxo*cyclo*hexanecarboxylate (70 g.) in tetrahydrofuran (100 c.c.) was added dropwise during 40 min. The solution was heated under reflux for 1 hr., then treated cautiously with saturated aqueous ammonium chloride (400 c.c.). Isolation with ether followed by distillation gave the *ethynyl-alcohol* (60 g.), b. p. 158—159°/0·05 mm., n_D^{20} 1·5415 (Found: C, 72·4; H, 8·1. $C_{20}H_{26}O_4$ requires C, 72·7; H, 7·9%), ν 3510 s, 2220 w, and 1730 s cm.$^{-1}$, $\lambda_{max.}$ 243, 253, 289, 297 mμ (log ε 4·20, 4·22, 3·49, 3·50, respectively). Yields were lower when the reaction was carried out in ether without nitrogen.

Ethyl 2-*Hydroxy*-2-m-*methoxyphenethyl*-1 : 3-*dimethyl*cyclo*hexanecarboxylate* (II).—The above ethynyl-alcohol (20 g.) in ethyl acetate (120 c.c.) with 10% palladized charcoal (1 g.) absorbed 2 mols. of hydrogen. The product (19·7 g.), on distillation, gave the *phenethyl*cyclo*hexanol*, b. p. 157—160°(bath)/0·05 mm. (Found: C, 71·7; H, 9·1. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%), ν 3550 m, and 1725 s cm.$^{-1}$, $\lambda_{max.}$ 217, 273, 279·5 mμ (log ε 3·88, 3·31, 3·29, respectively).

Cyclization of the Hydroxy-ester (II).—(*A*) (cf. ref. 7). The preceding compound (10 g.) and phosphoric oxide (23 g.) were heated together at 12 mm., the temperature being raised to 145° during ½ hr. and kept at 140—145° for 1 hr. Ice was added to the cooled mixture, which was then made alkaline with 2N-sodium hydroxide. The product, a brown oil (7 g.), was isolated with ether. The combined products from several such experiments were distilled to give a yellow, viscous oil with a blue fluorescence, b. p. 100—180°/0·15 mm. Chromatography of the oil (10 g.) on alumina (1·5 kg.) and elution with 9 : 1 light petroleum–benzene (8·25 l.) gave a yellow oil (1·69 g.), shown by its infrared absorption spectrum to contain no ethoxycarbonyl group, and to be similar to the product of cyclization of the hydroxy-ester (II) with polyphosphoric acid (below). Elution with 1 : 1 light petroleum–benzene (2·25 l.) gave semisolid material (fraction 1) (5·11 g.); further elution with the same solvent (3 l.) and then benzene (1·5 l.) gave an oil (fraction 2) (2·78 g.). Chromatography of fraction 1 on alumina (1·5 kg.) and elution with 3 : 1 light petroleum–benzene (1·5 l.) gave ester C (0·15 g.). Elution with 1 : 1 light petroleum–benzene (0·75 l.) gave semisolid material (fraction 3) (0·93 g.); the same solvent (3 l.) eluted ester A (3·02 g.), m. p. 69—72°, and then (1·5 l.) semisolid material (fraction 4) (0·36 g.). Successive elution with this solvent (1·5 l.) and benzene (2·25 l.) gave ester B (0·43 g.) as an oil. Chromatography of fraction 3 on alumina (300 g.) in a similar manner gave ester C (0·17 g.), a mixture of esters A and C (0·28 g.), and ester A (0·41 g.). Fractions 2 and 4 were combined and chromatographed on alumina (1 kg.). Elution with 1 : 1 light petroleum–benzene (1·5 l.), then 1 : 2 light petroleum–benzene (0·75 l.) gave a mixture of esters A and B (fraction 5) (1·03 g.): the last solvent mixture (5·25 l.) eluted ester B (2·07 g.). Chromatography of fraction 5 gave ester A (0·30 g.), a mixture of A and B (0·05 g.), and ester B (0·63 g.).

Ester A (3·73 g.) was identified as *ethyl* 1 : 2 : 3 : 4 : 9 : 10 : 11α : 12-*octahydro*-7-*methoxy*-1α : 12β-*dimethylphenanthrene*-1β-*carboxylate* (V; R = Et), m. p. 73—74° [from light petroleum (b. p. 40—60°)] (Found: C, 76·1; H, 8·7. $C_{20}H_{28}O_3$ requires C, 75·9; H, 8·9%), $\lambda_{max.}$ 219·5, 277, 285 mμ (log ε 3.96, 3·30, 3·31, respectively). Ester B (3·13 g.) was identified as *ethyl* 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-7-*methoxy*-1ξ : 12β-*dimethylphenanthrene*-1ξ-*carboxylate* (VI; R = CO_2Et), b. p. 146—150°/0·25 mm. (Found: C, 76·1; H, 9·3%), $\lambda_{max.}$ 219·5, 277·5, 284·5 mμ (log ε 3·89, 3·27, 3·26, respectively). Ester C, identified as ethyl 2-*m*-methoxyphenethyl-1 : 3-dimethyl*cyclo*hex-2-enecarboxylate (IV), had b. p. 152—155° (bath)/0·3 mm. (Found: C, 75·5; H, 8·8. Calc. for $C_{20}H_{28}O_3$: C, 75·9; H, 8·9%), ν 1728 s, 1134 m, 1080 m, 776 m, 741 m cm.$^{-1}$, $\lambda_{max.}$ 273, 279·5 mμ (log ε 3·09, 3·12, respectively) (cf. Haworth and Moore [1]).

(*B*) (cf. ref. 2). The hydroxy-ester (II) (0·55 g.) was stirred under nitrogen with a solution of phosphoric oxide (30 g.) in 88—90% orthophosphoric acid (25 c.c.) at 80—85° for 45 min. Some effervescence was observed during the first few minutes. The mixture was poured into ice and water, and the oil was collected with ether. The ethereal solution was washed with brine, 2N-sodium hydroxide, and water, dried, and evaporated to give a brown, viscous oil (0·33 g.), shown by its infrared spectrum to contain no ethoxycarbonyl group. Acidification of the alkaline washings gave a negligible quantity of acid. The oil (0·57 g.) obtained in a similar experiment was chromatographed on alumina (50 g.). Elution with 1 : 1 light petroleum–benzene (250 c.c.) and distillation gave a mixture of hexahydro-7-methoxy-1 : 12-dimethylphenanthrenes (0·23 g.), b. p. 140°(bath)/0·05 mm. (Found: C, 84·1, 84·9; H, 9·1, 9·4. Calc. for $C_{17}H_{22}O$: C, 84·3; H, 9·2%), ν 1240 s, 1030 ms, 848 m, 810 m cm.$^{-1}$, $\lambda_{max.}$ 227, 261 mμ (log ε 4·33, 3·80, respectively).

XUM

This mixture did not absorb hydrogen in the presence of Adams catalyst. In ethyl acetate over 5% palladized charcoal it absorbed 0·4 mol. of hydrogen: in ethanol containing a trace of perchloric acid and with 10% palladized charcoal it absorbed 0·3 mol. of hydrogen.

Similar results were obtained when the cyclization was performed with polyphosphoric acid at 100° and at 120°.

Cyclization of Ethyl 2-m-*Methoxyphenethyl*-1 : 3-*dimethyl*cyclo*hex*-2-*enecarboxylate* (IV).—(*A*). The reaction between the ester (43 mg.) and phosphoric oxide (300 mg.), carried out under the conditions used for the cyclization (*A*) of the hydroxy-ester (II), gave a crude product (31 mg.) shown by comparison of infrared spectra to be similar in composition to the crude product of the latter reaction.

(*B*). The ester (30 mg.) was treated with polyphosphoric acid under the conditions used for the cyclization (*B*) of the hydroxy-ester (II). The crude product (21 mg.) was shown by its infrared spectrum to contain no ethoxycarbonyl group and to be identical with the product obtained from the hydroxy-ester.

Action of Polyphosphoric Acid on Esters of Tricyclic, Tertiary Acids.—The distilled mixture of esters A and B from the cyclization (*A*) of the hydroxy-ester (II), treated at 80—85° or at 100° with polyphosphoric acid as in the cyclization (*B*) of the preceding paragraph, gave a crude product containing no ethoxycarbonyl group and spectroscopically identical with the product obtained from the two cyclizations (*B*).

Methyl *O*-methylpodocarpate likewise gave a product containing no methoxycarbonyl group under these conditions.

Hydrolysis of Esters A and B.—(i) Ester B (574 mg.) was heated under reflux for 5 hr. with a solution of potassium hydroxide (5 g.) in ethylene glycol (15 c.c.) and water (5 c.c.) which had previously been boiled until the temperature of the liquid reached 150°. Dilution with water, followed by the usual acid–alkali treatment, gave unhydrolysed ester (28 mg.) and crystalline 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-7-*methoxy*-1ξ : 12-*dimethylphenanthrene*-1ξ-*carboxylic acid* (VI; R = CO_2H) (456 mg.), which was sufficiently pure for further reactions. Recrystallized twice from methanol, it had m. p. 192—193·5° (Found: C, 74·8; H, 8·4. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4%). The *methyl ester*, obtained by treatment of the acid with diazomethane, had b. p. 138—140° (bath)/0·15 mm. (Found: C, 75·7; H, 8·3. $C_{19}H_{26}O_3$ requires C, 75·5; H, 8·7%).

Hydrolysis of ester A by this procedure gave a 35% yield of the crude, resinous acid. When the reaction time was extended to 12 hr., the yield was increased to 74%. On treatment with diazomethane, the acid gave the *methyl ester*, which, after filtration through alumina, crystallized from light petroleum as needles, m. p. 107·5—108·5° (Found: C, 75·5; H, 8·7%).

(*B*) (cf. ref. 19). The ester (*ca.* 70 mg.) was heated at 150° for 4 hr. in a sealed tube with 2 c.c. of a solution of potassium hydroxide (5 g.) in ethanol (15 c.c.) and water (5 c.c.). The acid and unchanged ester were isolated in the usual way. The yield of acid from ester A was 24%, from ester B 59%.

16-*Hydroxypodocarp*-8-*en*-7-*one* (I; R = CH_2·OH) (cf. ref. 11).—To a stirred solution of ester A (V; R = Et) (2·5 g.) in dry dioxan (50 c.c.), dry ethanol (250 c.c.), and liquid ammonia (*ca.* 500 c.c.) were added lithium (27·5 g.) in thin strips, dry ethanol (300 c.c.), and further portions (each *ca.* 50 c.c.) of liquid ammonia at such a rate as to maintain the lithium-rich phase which formed bronze-red globules on the surface. After the addition, which required *ca.* 45 min., stirring was continued until the bronze layer disappeared (*ca.* 10 min.). Brine (1 l.) and ether were then added, followed by sufficient water to dissolve the inorganic material. The product, isolated with ether, was a resin (2·1 g.) [ν (in CS_2) 3623 w, 1698 m, 1653 w, 1224 s, 1020 s, 784 m cm.$^{-1}$]. Acidification of the aqueous phase followed by extraction with ether gave no acid. The solid was heated at 70° for 1 hr. with ethanol (50 c.c.) and 5 c.c. of a solution of concentrated hydrochloric acid (5 c.c.) in water (2·5 c.c.) and ethanol (2·5 c.c.). After dilution with water and extraction with ether, the combined organic solutions were washed with brine, dried, and evaporated to give a pale fawn, solid (1·8 g.). The material (3 g.) obtained from this and a similar experiment gave, on recrystallization from ethyl acetate, 16-*hydroxypodocarp*-8-*en*-7-*one* (2·1 g.), as laths, m. p. 187—191°. Recrystallized again for analysis it had m. p. 190—191° (Found: C, 77·8; H, 10·2. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%), ν (in Nujol) 3390 s, 1650 s, 1613 m; (in CS_2) 3610 w, 1678 s cm.$^{-1}$, $\lambda_{max.}$ 241 mμ (log ε 4·23). When recrystallized from methanol, the compound retained solvent tenaciously and was

[19] Sherwood and Short, *J.*, 1938, 1010.

XUM

not obtained analytically pure. The deep red 2 : 4-*dinitrophenylhydrazone*, recrystallized twice from chloroform–methanol, had m. p. 219—220° (Found: C, 60·4; H, 6·8; N, 11·4. $C_{23}H_{30}O_5N_4,CH_3{\cdot}OH$ requires C, 60·7; H, 7·2; N, 11·8%).

The mother-liquors from the recrystallization of the hydroxy-ketone were evaporated, and the residue was chromatographed on deactivated alumina (100 g.). Elution with benzene (500 c.c.) gave non-ketonic material (0·64 g.); 9 : 1 benzene–ether (300 c.c.) eluted a solid $\beta\gamma$-unsaturated ketone (0·15 g.), ν 1709 cm.$^{-1}$ (non-conjugated C=O). Elution with the same solvent (100 c.c.) and then 1 : 1 benzene–ether (100 c.c.) gave, after recrystallization from ethyl acetate, 16-hydroxypodocarp-8-en-7-one (100 mg.).

The $\beta\gamma$-unsaturated ketone eluted from the column was isomerized to the hydroxy-ketone (I; R = $CH_2{\cdot}OH$) on treatment with ethanolic hydrochloric acid under the conditions described above for the conversion of the crude reduction product into the hydroxy-ketone.

The aromatic ring of ester A could not be reduced by milder methods; the results were similar to those obtained in the reduction of the methyl ester (VI; R = CO_2Me).

7-*Oxopodocarp*-8-*en*-16-*oic Acid* (I; R = CO_2H).—(*A*). The preceding hydroxy-ketone (2·17 g.) in glacial acetic acid (50 c.c.) was treated portionwise at room temperature with a 2% solution of chromium trioxide in acetic acid (74 c.c.) and then set aside for 2 hr. The acetic acid was removed *in vacuo*, and water and ether were added to the residue. The layers were separated, and the aqueous layer was extracted with ether. The combined ethereal solutions were washed with water, 2N-sodium carbonate, and water again, then dried and evaporated to give a yellow solid (0·52 g.). Acidification of the carbonate washings, and extraction with ether, afforded 7-*oxopodocarp*-8-*en*-16-*oic acid* (1·12 g.). Reoxidation of the neutral material with chromium trioxide solution gave more of the crude keto-acid (0·21 g.). After recrystallization from ethanol, the keto-acid (1·04 g.) had m. p. 209—211°. Recrystallized again for analysis, it had m. p. 211—211·5° (Found: C, 73·8; H, 9·0. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%), ν (in Nujol) 1724 (CO_2H), 1640 ($\alpha\beta$-unsaturated ketone), 1621 cm.$^{-1}$ (C=C); (in $CHCl_3$) 1695, 1667 cm.$^{-1}$; $\lambda_{max.}$ 241 mμ (log ε 4·25).

(*B*). The acid (V; R = H) (190 mg.) was treated with lithium, ethanol, and liquid ammonia followed by ethanolic hydrochloric acid, as described for the reduction of ester A. The usual acid–alkali treatment gave neutral material (32 mg.), the spectrum of which [ν 1695 cm.$^{-1}$ (weak shoulder at 1739 cm.$^{-1}$)] did not resemble that of the hydroxy-ketone (I; R = $CH_2{\cdot}OH$). The resinous acid (110 mg.) gave, after decolorization with charcoal and two recrystallizations from ethanol, the keto-acid (I; R = CO_2H) (12 mg.), m. p. 209—211°, which was identified by infrared comparison and mixed m. p.

Methyl (±)-7-*Oxopodocarp*-8-*en*-16-*oate* (I; R = CO_2Me).—The preceding keto-acid (92 mg.) in dioxan (5 c.c.) was treated with an excess of ethereal diazomethane. After dilution with ether, the solution was washed with 2N-sodium carbonate and water, dried, and evaporated. The residue, which slowly crystallized, gave on recrystallization from light petroleum (b. p. 40—60°) *methyl* (±)-7-*oxopodocarp*-8-*en*-16-*oate* (45 mg.), m. p. 97—99°. Partial evaporation of the mother-liquors from the recrystallization gave a further crop (7 mg.). Chromatography of the uncrystallizable residue from the second recrystallization on deactivated alumina (2 g.), and elution with benzene (12 c.c.), gave the crystalline keto-ester (6 mg.). After a second recrystallization, the compound had m. p. 98—99° (Found: C, 74·3; H, 8·9. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%), $\lambda_{max.}$ 241 mμ (log ε 4·25). The *semicarbazone*, platelets from methanol, had m. p. 221·5° (Found: C, 65·8; H, 8·5; N, 12·1. $C_{19}H_{29}O_3N_3$ requires C, 65·7; H, 8·4; N, 12·1%).

The authentic (+)-keto-ester from agathenedicarboxylic acid,[4] recrystallized from light petroleum, had m. p. 119—120°, $\lambda_{max.}$ 241 mμ (log ε 4·25) [lit.,[4] m. p. 117°, $\lambda_{max.}$ 242 mμ (log ε 4·26)]. The infrared spectra (in CS_2) of this compound and the synthetic (±)-keto-ester were identical. The mixed m. p. lay between the m. p.s of the (+)- and the (±)-compound.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ-*hydroxymethyl*-1ξ : 12β-*dimethylphenanthren*-7-*one* (X; R = $CH_2{\cdot}OH$).—Ester B (0·61 g.) was treated with lithium, ethanol, and liquid ammonia as described for the reduction of ester A. The resinous dihydro-compound (0·53 g.) had infrared bands at 3361 s, 1701 ms, 1667 ms, 1214 s, 1031 s, and 785 ms cm.$^{-1}$. Treatment with ethanolic hydrochloric acid gave a resin (0·48 g.). On crystallization from ether it gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*dodecahydro*-1ξ-*hydroxymethyl*-1ξ : 12β-*dimethylphenanthren*-7-*one* (110 mg.), m. p. 154—158°, which separated from acetone in plates, m. p. 158—160° (Found: C, 78·0; H, 9·8. $C_{17}H_{26}O_2$ requires C, 77·8; H, 10·0%),

ν (in Nujol) 3400 s, 1658 s, 1618 m cm.$^{-1}$, $\lambda_{max.}$ 244 mμ (log ε 4·25). Chromatography of the residues from the crystallization on deactivated alumina (50 g.) and elution with 9 : 1 benzene–ether (200 c.c.) gave non-ketonic material (59 mg.). Further elution with the same solvent (150 c.c.) gave a resin (73 mg.) having infrared bands at 3413 s, 1724 s cm.$^{-1}$. Elution with 4 : 1 benzene–ether (150 c.c.) and recrystallization from ether gave more of the hydroxy-ketone (24 mg.).

Lithium Reduction under Milder Conditions (*cf. ref.* 9).—A solution of the methyl ester (VI; R = CO_2Me) (218 mg.) and lithium (130 mg., *ca.* 25 g.-atoms/mole) in dry ether (34 c.c.) and liquid ammonia (85 c.c.) was stirred vigorously for 15 min. Dry ethanol (1 c.c.) was then added during 15 min. When the blue colour had disappeared, water was added, and the mixture was extracted with ether. The ethereal solution was washed with water, dried, and evaporated to a pale yellow oil (140 mg.). The infrared absorption spectrum showed that no reduction of the aromatic ring had occurred; in confirmation of this, no ketonic material could be detected after treatment of the compound with ethanolic hydrochloric acid. Distillation of the crude product gave 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-1ξ-*hydroxymethyl*-7-*methoxy*-1ξ : 12β-*dimethylphenanthrene* (VI; R = CH_2·OH), b. p. 140—143°(bath)/0·1 mm. (Found: C, 78·2; H, 9·2. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·6%), ν 3356 s, 1241 s, 1036 s, 867 m, 844 m, 813 m cm.$^{-1}$.

Reduction of the methyl ester, the above alcohol, or of its tetrahydropyranyl ether under more forcing conditions gave essentially the same results, only traces of ketone being detected by infrared absorption after treatment of the reduction product with ethanolic hydrochloric acid. When this procedure was applied to acid B (VI; R = CO_2H), the acid was recovered in high yield, even after treatment with 200-g.-atoms of lithium. Other solvents (tetrahydrofuran and 1 : 2-dimethoxyethane) were used in some experiments, with the same results.

Oxidation of the Alcohol (VI; R = CH_2·OH).—The alcohol (51 mg.) in acetone (3 c.c.) was treated with aqueous 8N-chromic acid (0·1 c.c.). After 5 min., water and ether were added. The usual acid–alkali treatment gave neutral material (27 mg.) which had m. p. 98—100° after recrystallization from ethanol and ν (in CS_2) 2680 w and 1727 s, shoulder at 2860 cm.$^{-1}$ (aldehyde). The acidic material (8 mg.), after recrystallization from methanol, had m. p. 183—186°, but was shown by comparison of infrared spectra to be the acid (VI; R = CO_2H) (m. p. 192—193·4°). The neutral aldehydic oxidation product (7·6 mg.) was converted into the same acid (3·7 mg.) by oxidation with an excess of 8N-chromic acid. After recrystallization from aqueous methanol this had m. p. 187—191°, and was shown to be identical with an authentic sample by mixed m. p., and by infrared comparison.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ : 12β-*dimethyl*-7-*oxophenanthrene*-1ξ-*carboxylic Acid* (X; R = CO_2H).—The hydroxy-ketone (X; R = CH_2·OH) (108 mg.), oxidized with 2% chromium trioxide solution under the conditions described for the oxidation of the isomeric hydroxyketone (I; R = CH_2·OH), gave the *keto-acid* (65 mg.). Recrystallized twice from ether, the compound formed elongated plates, m. p. 172—173·5° (Found: C, 73·4; H, 8·7. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%), ν (in Nujol) 1733 s and 1681 s cm.$^{-1}$, $\lambda_{max.}$ 242 mμ (log ε 4·24).

Methyl 1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11β : 12 : 13ξ-*Dodecahydro*-1ξ : 12β-*dimethyl*-7-*oxophenanthrene*-1ξ-*carboxylate* (X; R = CO_2Me).—The above crude keto-acid (45 mg.) in dioxan (3 c.c.) was esterified by an excess of ethereal diazomethane. The oil (42 mg.) was chromatographed on deactivated alumina (5 g.). Elution with benzene (40 c.c.) gave the *keto-ester* (25 mg.) which crystallized when scratched (m. p. 96—104°). It crystallized from light petroleum as needles, m. p. 106—107° (Found: C, 74·4; H, 9·0. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%), $\lambda_{max.}$ 243 mμ (log ε 4·21). The *semicarbazone*, recrystallized twice from methanol, had m. p. 208° (Found: C, 65·7; H, 8·3. $C_{19}H_{29}O_3N_3$ requires C, 65·7; H, 8·4%).

The infrared spectra (in CS_2) of this compound and of the (+)-keto-ester (VIII) from *neo*-abietic acid,[5] which had m. p. 128—130° (lit., 127—128°), showed considerable differences. The mixed m. p. was considerably lower than the m. p. of either compound.

Chromic Acid Oxidation of Ester B (VI; R = CO_2Et) (*cf. ref.*13).—To a solution of ester B (470 mg.) in glacial acetic acid (5 c.c.) were added 2·2 c.c. of a solution of chromium trioxide (2 g.) in 80% acetic acid (10 c.c.). After 18 hr. at room temperature, the solution was diluted with brine and extracted with chloroform. The organic solution was washed with 5% sodium hydroxide solution and water, dried, and evaporated to give a viscous, brown oil (320 mg.). Chromatography on alumina (30 g.) and elution with benzene (200 c.c.) gave starting material

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(84 mg.); 3 : 1 benzene–ether (200 c.c.) eluted *ethyl* 1 : 2 : 3 : 4 : 9 : 10 : 11β : 12-*octahydro*-7-*methoxy*-1ξ : 12β-*dimethyl*-9-*oxophenanthrene*-1ξ-*carboxylate* (XII) (52 mg.), b. p. 140—145° (bath)/0·05 mm. (Found: C, 72·6; H, 8·1. $C_{20}H_{28}O_4$ requires C, 72·7; H, 7·9%), ν 1725 s, 1686 s, 1245 s, 1034 ms, 873 w, 826 w cm.$^{-1}$, $\lambda_{max.}$ 223, 258, 325 mμ (log ε 4·34, 4·00, 3·45 respectively). Acidification of the alkali washings of the chloroform extracts gave a brown oil (50 mg.), which had a rather broad infrared band at 1725 cm.$^{-1}$ (cf. ref. 13).

We are grateful to Professors O. Jeger and L. Ruzicka for a sample of the (+)-keto-ester (I; R = CO_2Me), and to Drs. T. F. Sanderson and W. Hoehn for the (+)-keto-ester (VIII). One of us (A. C. D.) thanks the Department of Scientific and Industrial Research for a Maintenance Allowance.

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135. *Polyphenylethylenes. Part I. Preparation and Characteristics of Tetra*-p-*nitrophenylethylene.*

By John H. Gorvin.

Methods are described for the preparation of authentic tetra-*p*-nitrophenylethylene. In this compound the ethylenic linkage is of low reactivity but oxidation with chromium trioxide has given the epoxide, which rearranges to the pinacone under strongly acidic conditions. Tetra-*p*-aminophenylethylene has been characterised.

By treatment of tetraphenylethylene with nitric acid (*d* 1·48) for 3 hr., Biltz [1] obtained a substance, m. p. *ca.* 100°, which he was unable to purify: on the basis of nitrogen content he considered this a tetranitro-derivative. A crystalline oxidation product, m. p. 294°, appeared to be the corresponding epoxide. Wizinger [2] accepted the nitration product as tetra-*p*-nitrophenylethylene and claimed to have reduced it to tetra-*p*-aminophenylethylene, m. p. 250°, which he also prepared from 4 : 4′-diaminobenzophenone. Bassett, Thorne, and Young [3] obtained Biltz's nitration product in yellow crystals, m. p. 274—276°, but reported no analytical figures. By the action of dinitrogen tetroxide on tetraphenylethylene Schlenk [4] obtained a compound, m. p. 292°, which he presumed identical with Biltz's epoxide.

An approach to the unambiguous preparation of these compounds was suggested by the availability of α-bromination products of di-*p*-nitrophenylmethane.[5]

Authentic tetra-*p*-nitrophenylethylene, m. p. 298—299°, was obtained in 80% yield from dibromodi-*p*-nitrophenylmethane by the action of sodium iodide in acetone (cf. Finkelstein [6]) or pyridine. Di-*p*-nitrophenylmethyl bromide reacted in acetone, to give 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane, which Biltz [1] obtained by nitration of 1 : 1 : 2 : 2-tetraphenylethane.

The ethylene was obtained from di-*p*-nitrophenylmethyl bromide by the action of sodium methoxide in methanol, presumably by a route analogous to that of self-alkylations discussed by Hauser *et al.*,[7] but a concurrent reaction led to 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane. The reaction of sodium methoxide with dibromodi-*p*-nitrophenylmethane gave some tetra-*p*-nitrophenylethylene in addition to the expected dimethoxydi-*p*-nitrophenylmethane.

The structure of the ethylene was confirmed by its formation from tetraphenylethylene

[1] Biltz, *Annalen*, 1897, **296**, 219.
[2] Wizinger, *Ber.*, 1927, **60**, 1377.
[3] Bassett, Thorne, and Young, *J.*, 1949, 85.
[4] Schlenk, *Annalen*, 1913, **394**, 214.
[5] Gorvin, *J.*, 1955, 83.
[6] Finkelstein, *Ber.*, 1910, **43**, 1528, 1533.
[7] Hauser, Brasen, Skell, Kantor, and Brodhag, *J. Amer. Chem. Soc.*, 1956, **78**, 1653; Brasen, Kantor, Skell, and Hauser, *ibid.*, 1957, **79**, 397.

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by nitration under relatively mild conditions, preferably in an equipartite mixture of nitric acid (95%) and acetic acid. This was the most generally convenient preparation since it avoided the tedious purification of di-*p*-nitrophenylmethane:[8] moreover, tetraphenylethylene, in which *ortho*-nitration is reduced by steric compression, was readily accessible through a modification of Finkelstein's procedure. Nitration with dinitrogen tetroxide gave an identical product: no evidence was found for epoxidation in this reaction and it is probable that Schlenk's " epoxide "[4] was tetra-*p*-nitrophenylethylene.

In tetra-*p*-nitrophenylethylene the *p*-nitro-groups diminish the nucleophilic character of the central double bond, the reactivity of which is already reduced by conjugation[9] and the shielding effect of the bulky aryl groups.[10] Thus, whereas tetraphenylethylene fails to add bromine but reacts with chlorine[3,6] and with perbenzoic acid,[11] the tetra-*p*-nitro-derivative appeared to react with none of these and to be unaffected by dinitrogen trioxide, osmium tetroxide, selenium dioxide, lead tetra-acetate, and performic acid. The intense red colour shown in chlorosulphonic acid suggests the presence of a complex cation, but in this medium the nitro-groups must be extensively protonated.[12]

The ethylenic linkage was attacked by stronger oxidising agents: dinitrogen tetroxide reacted very slowly, to yield 4 : 4′-dinitrobenzophenone, permanganate readily gave the same product, but with chromium trioxide in acetic acid tetra-*p*-nitrophenyloxiran (28%) was formed in addition to the benzophenone. A non-cationic complex (cf. Zeiss and Zwanzig[13]) seems a rather more probable intermediate than a carbonium ion[14] in this instance: the epoxide may possibly be formed directly by a concurrent " three-centre-type "[15] addition, similar to that suggested for epoxidation by organic per-acids.[16] Tetra-*p*-nitrophenyloxiran appeared identical with the epoxide described by Biltz.[1] It was unusually stable in acidic media but concentrated sulphuric acid produced 1 : 2-rearrangement to *p*-nitrobenzoyltri-*p*-nitrophenylmethane. This pinacone was hydrolysed immediately in alcoholic potassium hydroxide to *p*-nitrobenzoic acid and tri-*p*-nitrophenylmethane, of which the anion is deep violet.[17]

Tetra-*p*-nitrophenylethylene dissolved in concentrated nitric acid, presumably through solvation of the nitro-groups, but its stability in these solutions depended greatly on the acid concentration. Little reaction occurred in 70% nitric acid (*d* 1·42) even at 80°. In stronger nitric acids, composed largely of the rather stable monohydrate[18] H_2O,HNO_3 (>77·8%), a slow reaction proceeded at 0°, reflected in a depression in the m. p. of the largely unchanged substance recovered on dilution with water. In this concentration region (*ca.* 78—84%) nitric acid solutions at 0° reacted rapidly with tetraphenylethylene to give tetra-*p*-nitrophenylethylene, which suggested that with the more concentrated acid (" *d* 1·48," *i.e.*, *ca.* 84·5—87·5%) and extended time used by Biltz[1] an additional reaction occurred, leading to a complex product. It is proposed to discuss this later.

Tetra-*p*-aminophenylethylene, m. p. 325°, was readily prepared by reduction of tetra-*p*-nitrophenylethylene, tetra-*p*-nitrophenyloxiran, or 4 : 4′-diaminobenzophenone: its structure was confirmed by conversion into tetraphenylethylene and into 1 : 1 : 2 : 2-tetra-*p*-aminophenylethane.[1] There is no evidence available to explain the low m. p. (250°) reported by Wizinger.[2] Polynitro-compounds of low solubility, such as the epoxide, are conveniently reduced in refluxing hydriodic acid.

[8] Staedel, *Annalen*, 1894, **283**, 153.
[9] Coulson and Jacobs, *J.*, 1949, 2805.
[10] Szwarc and Leavitt, *J. Amer. Chem. Soc.*, 1956, **78**, 3590.
[11] Lévy and Lagrave, *Bull. Soc. chim. France*, 1928, **43**, 440.
[12] Gillespie, *J.*, 1950, 2542.
[13] Zeiss and Zwanzig, *Chem. and Ind.*, 1956, 545; *J. Amer. Chem. Soc.*, 1957, **79**, 1733.
[14] Hickinbottom, Peters, and Wood, *J.*, 1955, 1360; Davis and Hickinbottom, *J.*, 1958, 2205.
[15] Skell and Garner, *J. Amer. Chem. Soc.*, 1956, **78**, 5430.
[16] Lynch and Pausacker, *J.*, 1955, 1525.
[17] Hawthorne and Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 2549.
[18] Chédin, Fénéant, and Vandoni, *Compt. rend.*, 1948, **226**, 1722; cf. Gillespie and Millen, *Quart. Rev.*, 1948, **2**, 277.

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In the usual screening tests, tetra-*p*-aminophenylethylene showed no antibacterial, antiprotozoal, or schistosomicidal activity.

Experimental

Concentrations of nitric acid are expressed in g. of acid per 100 g. of solution.

Debrominations with Sodium Iodide.—(a) *Dibromodiphenylmethane.* To diphenylmethane (33·6 g.) was added bromine (70 g.) during 3 hr. at 120° under illumination (incandescent lamp, 200 w). The product was refluxed with sodium iodide (80 g.) in acetone (400 c.c.) for 1½ hr. The filtered precipitate was washed with acetone, acidified aqueous sodium sulphite, and water and crystallised from dioxan–ethanol. This procedure, a modification of that of Finkelstein,[6] provided a rapid and convenient route to tetraphenylethylene (*ca.* 35%, m. p. 222°).

(b) *Dibromodi*-p-*nitrophenylmethane.* Di-*p*-nitrophenylmethane was treated with an excess of bromine in boiling carbon tetrachloride (20 vols.) under illumination (200 w) for 5 hr. The solution was evaporated to dryness and the residue refluxed for 1 hr. in acetone (20 vols.) with excess of sodium iodide. By addition of acidified aqueous sodium sulphite to the concentrated solution and crystallisation of the precipitate from dioxan or from acetic acid (extractor), *tetra*-p-*nitrophenylethylene* (*ca.* 80%) was obtained in yellow prismatic needles, m. p. 298—299° [306—307° (corr.)] (Found: C, 60·8; H, 3·3; N, 11·0. $C_{26}H_{16}O_8N_4$ requires C, 60·95; H, 3·1; N, 10·9%). These formed orange-red solutions in concentrated sulphuric acid and intensely red solutions in chlorosulphonic acid; the ethylene was recovered unchanged on addition to ice.

When dibromodi-*p*-nitrophenylmethane was treated with sodium iodide in moist pyridine (25 vols.) the resulting tetra-*p*-nitrophenylethylene (84%) was accompanied by 4 : 4′-dinitrobenzophenone (11%) formed by hydrolysis. The use of glacial acetic acid as solvent gave a mixture of 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane (*ca.* 55%) (see below) and di-*p*-nitrophenylmethane.

(c) *Di*-p-*nitrophenylmethyl bromide.* When the bromide was refluxed for 3 hr. with sodium iodide in acetone the main product was 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane (40%), which crystallised in needles, m. p. 330—335° (decomp.), from pyridine–ethanol and was identical with authentic material, m. p. 330—335° (decomp.) (Found: C, 60·9; H, 3·7; N, 10·9. Calc. for $C_{26}H_{18}O_8N_4$: C, 60·7; H, 3·5; N, 10·9%), prepared by nitration of 1 : 1 : 2 : 2-tetraphenylethane.[1] Di-*p*-nitrophenylmethane (19%) was also obtained.

When the solvent was glacial acetic acid, the product consisted of di-*p*-nitrophenylmethane (62%) and a small amount of polymeric material.

Alkaline Debrominations.—(a) *Di*-p-*nitrophenylmethyl bromide.* When sodium methoxide (from 0·5 g. of sodium) was added to the bromide (3·37 g.) in refluxing methanol the mixture developed an intense violet colour. This soon changed to brown and within 1 hr. a crystalline solid was precipitated, which gave tetra-*p*-nitrophenylethylene (35—40%) and the almost insoluble 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane (6—12%) on extraction with hot acetic acid.

Potassium hydroxide in methanol gave qualitatively similar results but in certain reactions the yield of the ethane was as high as 37% without corresponding increase in the yield of the ethylene.

(b) *Dibromodi*-p-*nitrophenylmethane.* The bromo-compound (0·416 g.) was refluxed with potassium hydroxide (0·26 g.) in methanol for 7 hr. The product obtained on dilution with water crystallised from acetic acid. A small yield of tetra-*p*-nitrophenylethylene was obtained, but the main product was *dimethoxydi*-p-*nitrophenylmethane* (35%) which formed large rhombs, m. p. 157—158° (Found: C, 56·9; H, 4·2; N, 8·8. $C_{15}H_{14}O_6N_2$ requires C, 56·6; H, 4·4; N, 8·8%). This was hydrolysed by concentrated sulphuric acid to 4 : 4′-dinitrobenzophenone.

Nitration of Tetraphenylethylene.—(*a*) To a mixture of 95% nitric acid (100 c.c.) and glacial acetic acid (100 c.c.) at 0—5° was added tetraphenylethylene (10 g.) in portions. After 1½ hr. the solution was diluted with water, and the precipitate collected, dried, and crystallised from dioxan, to give tetra-*p*-nitrophenylethylene (65—70%), m. p. 298—299° unchanged by admixture with previously described material.

(*b*) Nitration with dinitrogen tetroxide [19] according to Schlenk's method [4] gave an identical product (75%).

[19] Schlubach and Rott, *Annalen*, 1955, **594**, 65.

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(*c*) Aqueous nitric acid (79%, 83%, and 87% severally) (15 c.c.) reacted with tetraphenylethylene (1·0 g.) at 0—5° at progressively faster rates to give orange-yellow solutions. The products obtained on dilution with water (after 1 hr., 20 min., and 10 min.) gave tetra-*p*-nitrophenylethylene (>50%). If the 87% acid was allowed to react for 3 hr. at 0° the solution gave on dilution a complex mixture from which the ethylene was isolated with difficulty and in an impure state (*ca.* 20%).

Oxidation of Tetra-p-*nitrophenylethylene.*—(a) *Chromium trioxide.* The ethylene (0·5 g.) was heated in acetic acid (80 c.c.) with chromium trioxide (0·5 g.) at 90—100° for 3 hr. Crystals of tetra-*p*-nitrophenyloxiran (0·14 g., 28%) separated slowly from the cooled solution; these were recrystallised from dioxan or acetic acid and formed pale yellow prisms, m. p. 294—296° (decomp.) [301—303° (corr.)] (Found: C, 59·05; H, 3·1; N, 10·3. Calc. for $C_{26}H_{16}O_9N_4$: C, 59·1; H, 3·05; N, 10·6%). Biltz [1] gave m. p. 294° [298—299° (corr.)]. The major product, obtained by dilution with water and crystallisation from acetic acid, was 4 : 4′-dinitrobenzophenone (63%). The crude products gave no colour when treated, in dioxan solution, with ethanolic potassium hydroxide.

(b) *Potassium permanganate.* In acetone solution the only product found was 4 : 4′-dinitrobenzophenone.

(c) *Dinitrogen tetroxide.* The ethylene (0·5 g.) was kept in a sealed tube at 0° in dinitrogen tetroxide [19] (10 c.c.). After 9 months it was still largely unchanged: 4 : 4′-dinitrobenzophenone (*ca.* 25%) was the only product found.

Rearrangement of Tetra-p-*nitrophenyloxiran.*—When the orange-yellow solution of the epoxide in concentrated sulphuric acid was left for 2 hr., p-*nitrobenzoyltri*-p-*nitrophenylmethane* was obtained on addition to ice. Crystallisation always gave solvated material, probably of clathrate nature, which lost weight slowly and incompletely when heated under reduced pressure. Dioxan gave rhombs, m. p. 188—190° (decomp.) (Found: C, 58·8; H, 3·4; N, 9·2. $C_{26}H_{16}O_9N_4,C_4H_8O_2$ requires C, 58·4; H, 3·9; N, 9·1%) (the solvate possibly contained <1 mol. of dioxan as the nitrogen analysis is unreliable): acetic acid gave crystals, m. p. 179—181° (decomp.) [Found: C, 57·7; H, 3·2; N, 10·0; AcOH, 6·7 (by titration), 6·1 (loss at 150—160°/1·5 mm. in 40 hr.). $C_{26}H_{16}O_9N_4,\frac{2}{3}C_2H_4O_2$ requires C, 57·8; H, 3·3; N, 9·9; AcOH, 7·0%]. A solution in dioxan–ethanol became intensely violet on addition of alcoholic potassium hydroxide; the colour disappeared on dilution with water and acidification. A solid was filtered off after the acidified solution had been made slightly alkaline, and the filtrate was reacidified and extracted twice with ether. *p*-Nitrobenzoic acid, m. p. 235—236°, was obtained from the ether by extraction with 4% sodium hydroxide solution, which was then acidified. The solid was crystallised from chloroform–ether and then from chloroform, to give tri-*p*-nitrophenylmethane, m. p. 212°, not depressed by authentic material obtained by nitration of triphenylmethane.[20] The pinacone was unaffected by chromium trioxide in acetic acid.

The epoxide was also converted into the pinacone when its orange-red solution in chlorosulphonic acid was left for 2 hr., or when it was refluxed for 1½ hr. in glacial acetic acid (20 vols.) and concentrated sulphuric acid (10 vols.). In 95% nitric acid there was no appreciable change after 24 hr. at 0°: after 25 days, 4 : 4′-dinitrobenzophenone was recovered. In 100% nitric acid, some epoxide remained after 7 days, and the benzophenone was also present, but no colour was shown with alcoholic potassium hydroxide.

Tetra-p-*aminophenylethylene.*—(*a*) 4 : 4′-Diaminobenzophenone (0·5 g.) in concentrated hydrochloric acid (18 c.c.) was heated for 5 hr. with granulated tin. The crystals which separated were washed with ethanol and decomposed with aqueous sodium hydroxide, to give *tetra*-p-*aminophenylethylene* as a pale yellow crystalline substance becoming green in moist air: it showed a pale green fluorescence in ultraviolet light. When purified through its ethanol-insoluble tetrahydrochloride and crystallised from ethanol (extractor) it had m. p. 325° [333—334° (corr.)] (Found: C, 79·0; H, 6·2; N, 14·3. $C_{26}H_{24}N_4$ requires C, 79·6; H, 6·2; N, 14·3%). The *tetra*-N-*acetyl derivative* had m. p. 320° (from acetic acid) (Found: C, 71·7; H, 5·8; N, 9·8. $C_{34}H_{32}O_4N_4,0{\cdot}5H_2O$ requires C, 71·7; H, 5·8; N, 9·8%).

(*b*) An identical tetra-amine was obtained by the reduction of either tetra-*p*-nitrophenylethylene or the oxiran with tin or stannous chloride in hydrochloric acid.

(*c*) When tetra-*p*-nitrophenyloxiran was refluxed for 2½ hr. in hydriodic acid, and the solution was added to aqueous sodium sulphite, tetra-*p*-aminophenylethylene was precipitated on addition of alkali.

[20] Shoesmith, Sosson, and Hetherington, *J.*, 1927, 2221.

XUM

Tetra-*p*-aminophenylethylene gave a small yield of tetraphenylethylene when its diazotised solution was refluxed with ethanol. Reduction of the base with sodium in pentyl alcohol gave 1 : 1 : 2 : 2-tetra-*p*-aminophenylethane, m. p. 270—272°, not depressed on admixture with the base, m. p. 272—274°, prepared by reduction of 1 : 1 : 2 : 2-tetra-*p*-nitrophenylethane according to Biltz's directions [1] [he gave m. p. 272° (corr.)] or by refluxing in hydriodic acid (Found: C, 79·2; H, 6·9; N, 13·9. Calc. for $C_{26}H_{26}N_4$: C, 79·2; H, 6·6; N, 14·2%). This tetra-amine, dried at 100°/0·05 mm., absorbed *ca.* $2H_2O$ reversibly from moist air.

The author thanks Messrs. K. Baker and A. G. Seaborn for experimental assistance and Mr. P. R. W. Baker for the microanalysis.

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136. *Nitrogenous Chelate Complexes of Transition Metals. Part I. The Constitution and Properties of the* 1 : 10-*Phenanthroline Complexes of Tervalent Gold.*

By C. M. HARRIS.

The structure of the 1 : 10-phenanthroline (phen) complexes of gold(III) halides has been investigated in nitrobenzene and acetone solutions by means of conductometric and spectrophotometric measurements. The low molecular conductivities of the compounds AuX_3,phen (X = Cl, Br) in these solvents are due to the rapid rearrangement of $2[Au(phen)X_2]^+ + 2X^- \rightleftharpoons [Au(phen)X_2]^+ + [AuX_4]^- +$ phen resulting from the ready reaction of halide with the dihalogeno-(1 : 10-phenanthroline)gold(III) ion in non-aqueous solution. A possible explanation of this is given in terms of the ability of gold(III) to utilise two additional $6p6d$ bonds perpendicular to its normal $5d6s6p^2$ planar arrangement.

THE molecular conductivities (see Table 1) of the tervalent gold complexes $[Au(phen)X_2]X$ (X = Cl, Br; phen = 1 : 10-phenanthroline) were recently found to be of the order of 16—17 mho in nitrobenzene (10^{-3}M to 5×10^{-4}M) at 25°. These are much less than the values, 25—35 mho, usually associated with uni-univalent electrolytes in this solvent under comparable conditions. Since then, the perchlorates $[Au(phen)X_2]ClO_4$ (X = Cl, Br) have been shown to possess molecular conductivities (see Table 1) having twice the value

TABLE 1. *Molecular conductivities* (Λ) *in nitrobenzene at* 25°.

Compound	Concn. (M)	Λ (mho)	Compound	Concn. (M)	Λ (mho)
$[Au(phen)Cl_2]Cl$	$5·85 \times 10^{-4}$	15·7	$[Au(phen)Cl_2][AuCl_4]$ ...	$5·7 \times 10^{-4}$	27·7
$[Au(phen)Br_2]Br$	$1·0 \times 10^{-3}$	16·9	$[Au(phen)Br_2][AuBr_4]$...	$7·0 \times 10^{-4}$	27·1
$[Au(phen)Cl_2]ClO_4$	$2·5 \times 10^{-4}$	33·0	$[PhenH][AuCl_4]$	$1·23 \times 10^{-3}$	29·7
$[Au(phen)Br_2]ClO_4$	$1·0 \times 10^{-3}$	33·1	$[PhenH][AuBr_4]$	$1·0 \times 10^{-3}$	33·0

TABLE 2. *Molecular conductivities in acetone at* 25°.

Compound	Concn. (M)	Λ (mho)	Compound	Concn. (M)	Λ (mho)
$[Au(phen)Cl_2]Cl$	$2·3 \times 10^{-4}$	52·5	$[Au(phen)Br_2][AuBr_4]$...	$1·0 \times 10^{-3}$	135
$[Au(phen)Br_2]Br$	$1·0 \times 10^{-3}$	55·4		$5·0 \times 10^{-4}$	192
$[Au(phen)Br_2]ClO_4$	$1·0 \times 10^{-3}$	153	$[NEt_4][AuBr_4]$	$5·0 \times 10^{-4}$	194
$[Au(phen)Cl_2][AuCl_4]$ ...	$2·5 \times 10^{-4}$	193	$Na[AuCl_4],2H_2O$	$3·0 \times 10^{-4}$	166

of these simple halides. This suggests that the gold(III) halide complexes, AuX_3,phen, are not completely present as dihalogeno-(1 : 10-phenanthroline)gold(III) ions and halide ions when dissolved in nitrobenzene.

A possible explanation of this conductivity difference between the halides $[Au(phen)X_2]X$

and the perchlorates $[Au(phen)X_2]ClO_4$ is the reaction in this solvent of halide ions with the complex gold cation thus:

$$[Au(phen)X_2]^+ + 2X^- \rightleftharpoons [AuX_4]^- + phen$$

This would satisfactorily account for the molecular conductivities of the simple halides being approximately half those of the perchlorates, since two moles of $[Au(phen)X_2]X$ would form one mole of $[Au(phen)X_2][AuX_4]$ and one mole of 1 : 10-phenanthroline. Foss

FIG. 1. FIG. 2.

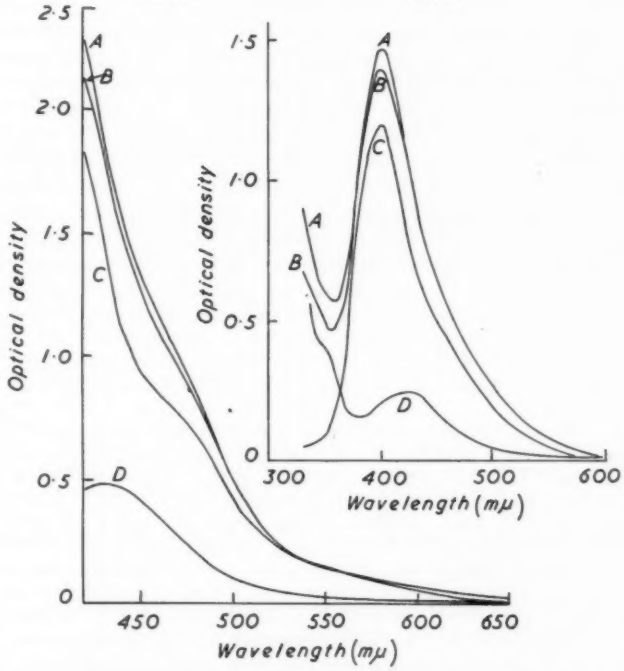


FIG. 1. *Absorption spectra of gold complexes in nitrobenzene* (1·33 *mm. cell*).
A. $3{\cdot}33 \times 10^{-3}$M-$[Au(phen)Br_2][AuBr_4]$ and also composite curve, $C + D$.
B. $6{\cdot}67 \times 10^{-3}$M-$Au(phen)Br_3$.
C. $3{\cdot}33 \times 10^{-3}$M-$[NEt_4][AuBr_4]$.
D. $3{\cdot}33 \times 10^{-3}$M-$[Au(phen)Br_2]ClO_4$.

FIG. 2. *Absorption spectra of gold complexes in acetone* (0·5 *cm. cell*).
A. 10^{-3}M-$Au(phen)Br_3$.
B. Composite curve, $C + D$.
C. 5×10^{-4}M-$[NEt_4][AuBr_4]$.
D. 5×10^{-4}M-$[Au(phen)Br_2]ClO_4$.

and Gibson [2] postulated this type of equilibrium in aqueous solution for 2 : 2′-dipyridyldiethylgold(III) bromide because they could isolate only the dibromodiethylaurate(III) derivative $[AuEt_2(dipy)][AuEt_2Br_2]$. Block and Bailar [1] have also observed that the 2 : 2′-dipyridyl compound $[Au(dipy)Cl_2]Cl$ could be prepared from alcohol solution only impure and is readily converted by water, or gentle heating, into the tetrachloroaurate(III) derivative, $[Au(dipy)Cl_2][AuCl_4]$. The 1 : 10-phenanthroline compounds, $[Au(phen)X_2]X$

[1] Block and Bailar, *J. Amer. Chem. Soc.*, 1951, **73**, 4722.
[2] Foss and Gibson, *J.*, 1949, 3063.

(X = Cl,Br), are not converted by water into the tetrahalogenoaurate(III) derivatives, $[Au(phen)X_2][AuX_4]$, and Block and Bailar were able to isolate the nitrate, $[Au(phen)Cl_2]NO_3$, from an aqueous solution of the chloride. The perchlorates, $[Au(phen)X_2]ClO_4$ (X = Cl, Br), were similarly prepared by the author.

The bromide $[Au(phen)Br_2]Br$ was examined spectrophotometrically in $6{\cdot}67 \times 10^{-3}$M-nitrobenzene in the range 4200—6500 Å (see Fig. 1). The shape of this curve is somewhat similar to that of the $[AuBr_4]^-$ ion which was measured in the form of the tetraethylammonium salt, $[NEt_4][AuBr_4]$, in $3{\cdot}33 \times 10^{-3}$M-solution. The dibromo-(1 : 10-phenanthroline)gold(III) ion, measured as its perchlorate in $3{\cdot}33 \times 10^{-3}$M-solution, absorbed at 4320 Å. The composite curve, constructed from the separate curves of the $[Au(phen)Br_2]^+$ and $[AuBr_4]^-$ ions, is almost identical with the absorption curve of $3{\cdot}33 \times 10^{-3}$M-$[Au(phen)Br_2][AuBr_4]$. This clearly supports the postulated equilibrium and indicates that in nitrobenzene the reaction is largely complete. Similar results were also obtained for 10^{-3}M-$[Au(phen)Br_2]Br$. These spectrophotometric measurements are further supported by the conductometric titration of $[Au(phen)Br_2]ClO_4$ with tetraethylammonium bromide in nitrobenzene. A sharp end-point (see Fig. 3), corresponding to the addition of 2 g.-ions of bromide to one of the complex gold(III) cation was obtained. That this equilibrium occurred with the chloride also, was demonstrated by a similar conductometric titration of the chloro-complex, $[Au(phen)Cl_2]ClO_4$, with triphenylmethylarsonium chloride (see Fig. 4). The chloro-compounds are not amenable to spectrophotometric

FIG. 3.

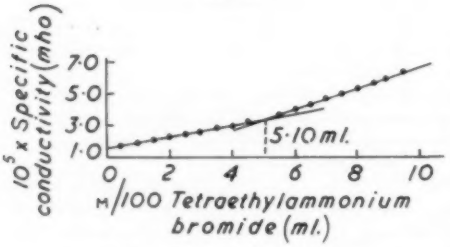
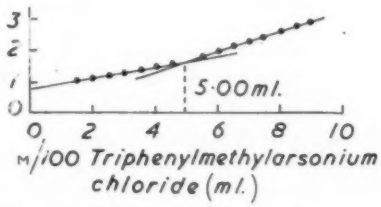


FIG. 4.



FIGS. 3 and 4. *Conductometric titrations of gold complexes in nitrobenzene at* 25°.

Fig. 3: Titration of 50 ml. of M/2000-$[Au(phen)Br_2]ClO_4$ by bromide.

Fig. 4: Titration of 1000 ml. of M/4000-$[Au(phen)Cl_2]ClO_4$ by chloride.

measurements in nitrobenzene since solvent absorption prevents measurements below 4200 Å.

The same type of equilibrium occurs with these compounds in acetone, as shown by their molecular conductivities (see Table 2). However, the solutions are not stable, and the compounds $[Au(phen)X_2]X$ appear to be slowly reduced since the solutions gradually fade. The bromide was examined spectrophotometrically in this solvent in the range 3300—6000 Å and, within the order of experimental error, a 10^{-3}M-solution of $[Au(phen)Br_2]Br$ gave a curve almost identical with that of a 5×10^{-4}M-solution of $[Au(phen)Br_2][AuBr_4]$ as well as a composite curve constructed from those for 5×10^{-4}M-$[NEt_4][AuBr_4]$ and 5×10^{-4}M-$[Au(phen)Br_2]ClO_4$ (see Fig. 2).

The fact that the equilibrium reaction with these gold(III) halide complexes of 1 : 10-phenanthroline occurs in acetone and nitrobenzene, and does not apparently take place to any extent in water, can be attributed to the higher solvation energies of the reacting ions in water than in either acetone of nitrobenzene. This type of equilibrium explains the failure of Block and Bailar [1] to obtain compounds with two molecules of phenanthroline per gold atom. Such compounds could presumably only be obtained in the

absence of halogens or other groups which show a similar tendency to co-ordinate to the gold(III) atom and replace the chelate.

The behaviour of these nitrogenous gold compounds can be compared with those of the isoelectronic platinum(II) and also with those of palladium(II). The ions $[Pd(chel)_2]^{2+}$ (chel = 1 : 10-phenanthroline or 2 : 2′-dipyridyl)[2a] and $[Pt(dipy)_2]^{2+}$ [2b] can be isolated as perchlorates or tetrachloroplatinates(II), whereas in the presence of chloride ions, they are readily converted into the non-electrolytes $[M(chel)X_2]$ (M = Pd, Pt).

Experimental

1 : 10-*Phenanthrolinium Tetrachloroaurate*(III).—1 : 10-Phenanthroline monohydrate (0·20 g.) dissolved in water (10 ml.) and 5N-hydrochloric acid (1·0 ml.) was treated with a solution of $NaAuCl_4.2H_2O$ (0·34 g.) in water (10 ml.) containing 5N-hydrochloric acid (1·0 ml.). The yellow precipitate was washed with water, acidified with a few drops of hydrochloric acid, and then with small amounts of 95% ethanol. The yellow microcrystalline compound was dried (P_2O_5) under vacuum (Found: C, 28·0; H, 1·9; Au, 37·8. $C_{12}H_9N_2Cl_4Au$ requires C, 27·7; H, 1·7; Au, 37·9%). The *compound* was soluble in acetone and ethanol forming yellow solutions.

1 : 10-*Phenanthrolinium Tetrabromoaurate*(III).—This *compound* was prepared similarly to the above chloro-compound. The deep red microcrystals were insoluble in water, soluble in acetone and slightly soluble in cold 95% ethanol (Found: C, 20·7; H, 1·4; Au, 28·2. $C_{12}H_9N_2Br_4Au$ requires C, 20·6; H, 1·3; Au, 28·2%).

Tetraethylammonium Tetrabromoaurate(III).—This *compound* was obtained as insoluble red microcrystals by mixing aqueous solutions of tetraethylammonium bromide and sodium tetrachloroaurate(III) dihydrate containing excess of potassium bromide. The precipitate was washed with cold water and dried (P_2O_5) (Found: C, 15·0; H, 2·9; Au, 30·4. $C_8H_{20}NBr_4Au$ requires C, 14·85; H, 3·1; Au, 30·5%).

Dichloro-(1 : 10-*phenanthroline*)*gold*(III) *Chloride*.—To a boiling solution of 1 : 10-phenanthroline monohydrate (0·55 g.) in water (40 ml.) was added sodium tetrachloroaurate(III) dihydrate (0·90 g.) in water (20 ml.), with stirring. The pale yellow precipitate of $[Au(phen)Cl_2][AuCl_4]$ which was first deposited, dissolved when boiled for a few min. The addition of finely powdered ammonium chloride (15 g.) then gave an immediate orange precipitate. The solution was stirred until all the ammonium chloride had dissolved, and then cooled to room temperature. The orange compound was filtered off and washed with small amounts of ethanol followed by dry ether; yield of vacuum-dried material, 0·80 g. (Found: Cl, 22·4; Au, 40·4. Calc. for $C_{12}H_8N_2Cl_3Au$: Cl, 22·0; Au, 40·8%). This compound was soluble in cold water, yielding an acid solution which turned blue litmus red.

Dichloro-(1 : 10-*phenanthroline*)*gold*(III) *Perchlorate*.—To an aqueous solution (25 ml.) of sodium tetrachloroaurate(III) dihydrate (0·40 g.) was added 1 : 10-phenanthroline monohydrate (0·26 g.), and the resulting mixture boiled for some minutes. The boiling solution was treated dropwise with a solution (5·0 ml.) of sodium perchlorate (2·0 g.). The yellow crystals were filtered off, and washed with distilled water and then small amounts of cold acetone, followed by dry ether; yield of vacuum-dried material, 0·27 g. (Found: C, 26·7; H, 1·8; N, 4·8; Au, 35·9. $C_{12}H_8O_4N_2Cl_3Au$ requires C, 26·3; H, 1·5; N, 5·1; Au, 36·0%).

Dibromo-(1 : 10-*phenanthroline*)*gold*(III) *Bromide*.—A solution of sodium tetrachloroaurate(III) dihydrate (4·0 g.) in water (100 ml.) was treated with 1 : 10-phenanthroline monohydrate (4·2 g.) in hot water (200 ml.). The clear solution was treated, while hot, with potassium bromide (5·0 g.) in the minimum amount of hot water. There was an immediate precipitate of dark reddish-brown crystals. On cooling, the compound was filtered off, washed with water, and dried at 100°; yield 5·7 g. (Found: Au, 31·7. Calc. for $C_{12}H_8N_2Br_2Au$: Au, 31·95%).

Dibromo-(1 : 10-*phenanthroline*)*gold*(III) *Perchlorate*.—A solution (600 ml.) of the preceding bromide (0·50 g.) in boiling water was treated with a hot solution (80 ml.) of ammonium perchlorate (12 g.). The dark yellow precipitate was filtered off from the cooled solution and washed well with cold water followed by small amounts of ethanol and dry ether; yield of

[2a] Livingstone, *J. Proc. Roy. Soc., N.S.W.*, 1951, **85**, 151; 1952, **86**, 32.
[2b] Morgan and Burstall, *J.*, 1934, 965.

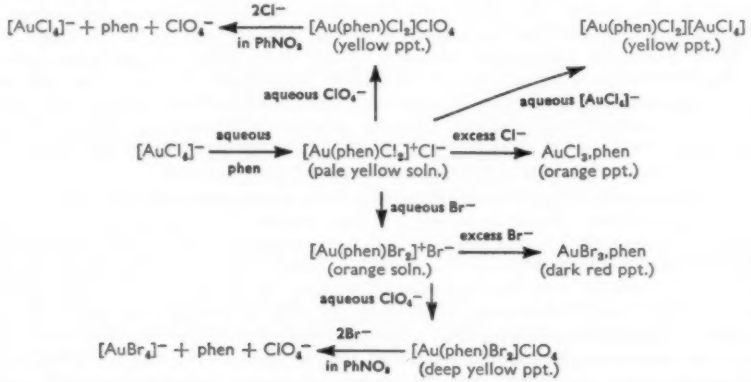
vacuum-dried material, 0·40 g. (Found: C, 23·1; H, 1·4; N, 4·5; Au, 31·5. $C_{12}H_8O_4N_2ClBr_2Au$ requires C, 22·6; H, 1·3; N, 4·4; Au, 31·0%).

Dichloro-(1 : 10-*phenanthroline*)*gold*(III) *Tetrachloroaurate*(III).—A boiling solution (50 ml.) of 1 : 10-phenanthroline monohydrate (0·20 g.) was treated dropwise with a hot solution (15 ml.) of sodium tetrachloroaurate(III) dihydrate (0·80 g.). After a few minutes' heating the yellow crystals were filtered off, and washed with cold water, absolute ethanol, and dry ether; yield of vacuum-dried material, 0·80 g. (Found: C, 18·5; H, 1·0; N, 3·7; Au, 49·9. Calc. for $C_{12}H_8N_2Cl_6Au_2$: C, 18·3; H, 1·0; N, 3·6; Au, 50·1%).

Dibromo-(1 : 10-*phenanthroline*)*gold*(III) *Tetrabromoaurate*(III).—A warm stirred solution of sodium tetrachloroaurate(III) dihydrate (1·0 g.) and sodium bromide (4·0 g.) in water (30 ml.) was treated slowly with a boiling solution (25 ml.) of 1 : 10-phenanthroline monohydrate (0·25 g.). The precipitate was filtered from the hot solution and washed with water followed by cold acetone. The acetone appeared to remove an orange compound and leave dark red microcrystals of the required *compound* (Found: C, 13·9; H, 0·8; Au, 37·4. $C_{12}H_8N_2Br_6Au_2$ requires C, 13·7; H, 0·8; Au, 37·42%).

Discussion

The reactions studied in this investigation are summarised below and provide an interesting example of the change in relative reactivity of complex ions on passing from aqueous to non-aqueous media. For example, the dihalogeno-(1 : 10-phenanthroline)-gold(III) ion can be readily obtained in aqueous solution by treating the tetrahalogenoaurate(III) ion with 1 : 10-phenanthroline, whereas in solvents of lower dielectric constant and smaller solvating ability, such as nitrobenzene and acetone, the $[Au(phen)X_2]^+$ ions (X = Cl, Br) readily pass to the $[AuX_4]^-$ ions (X = Cl, Br) in the presence of halide ions. The instantaneous nature of this reaction in non-aqueous solution, and the much deeper colour of the halides AuX_3,phen (X = Cl, Br) than of the corresponding perchlorates $[Au(phen)X_2]ClO_4$ (X = Cl, Br) in the solid state, call for comment.



Tervalent gold is usually square-co-ordinated in its compounds,[3,4,5] and this square-planar configuration together with the diamagnetism of gold(III) compounds is consistent with the use by gold of $5d6s6p^2$ bonds. Harris and Nyholm [6] have recently prepared sexicovalent gold(III) complexes of the type $[Au(diarsine)_2X_2]ClO_4$ (X = Br and I; and diarsine = *o*-phenylenebisdimethylarsine), and the formation of these complexes has been

[3] Wells, "Structural Inorganic Chemistry," Oxford Univ. Press, 1st Edn., 1947, p. 508; 2nd Edn., 1950, p. 625.
[4] Sidgwick, "The Chemical Elements and their Compounds," Clarendon Press, Oxford, 1950, Vol. 1, pp. 177—192.
[5] Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, 2nd Edn., 1948, pp. 100—102.
[6] Harris and Nyholm, *J.*, 1957, 63—70.

interpreted in terms of collinear $6p6d$ bonds from gold binding the two halogens at right angles to the $5d6s6p^2$ bond hybrids which hold the four arsenic atoms in a square plane. It is expected that this type of sexicovalent arrangement should be distorted with elongated gold-halogen bonds, owing to the repulsion effect of the filled $5d_{z^2}$ gold orbital normal to the plane of the square. This type of structure has been shown to occur with the diarsine complexes of Ni(II), Pd(II), and Pt(II) of general formula $[M(diarsine)_2X_2]$.[7] A distorted octahedral arrangement for gold(III) can also be seen in the structures of the intensely coloured complexes $Cs_2[AgCl_2][AuCl_4]$ and $Cs_2[AuCl_2][AuCl_4]$ studied by Elliot and Pauling.[8] Owing to packing in the crystal two additional Au(III)–Cl bonds are observed at 3·1 Å. These are perpendicular to the $[AuCl_4]^-$ plane which contains Au(III)–Cl bonds at 2·42 Å in length.

The reactions and colours of the 1 : 10-phenanthroline complexes studied in these investigations can be interpreted in terms of the formation of additional $6p_z6d_{z^2}$ collinear bonds at the gold(III) atom. For example, we believe that in view of the above discussion, the markedly deeper colour of the halides AuX_3,phen (X = Cl,Br) than of the corresponding perchlorates $[Au(phen)X_2]ClO_4$ (X = Cl,Br) is probably due to the presence in the crystal of two additional elongated gold · · · halogen bonds perpendicular to a planar dihalogeno-(1 : 10-phenanthroline)gold(III) ion, thus:

$$Au(phen)X_2 \cdot\cdot\cdot\cdot\cdot X \cdot\cdot\cdot\cdot Au(phen)X_2 \cdot\cdot\cdot\cdot\cdot X \cdot\cdot\cdot\cdot Au(phen)X_2 \cdot\cdot\cdot\cdot\cdot$$

This type of structure also gives a reasonable mechanism for the very rapid rearrangement of AuX_3,phen molecules in nitrobenzene and in acetone and for the conductometric titrations of the $[Au(phen)X_2]^+$ ions with halide ions in these solvents. The ready ionisation of these molecules in water to $[Au(phen)X_2]^+$ and X^- ions can be ascribed to the much greater solvation energy associated with water than with the non-aqueous solvents, nitrobenzene and acetone. Support for these ideas is provided by a recent spectrophotometric investigation of the reaction of the $[AuBr_4]^-$ ion with bromide ions in nitrobenzene;[9] this provides evidence that gold(III) can form a higher sexicovalent complex similar to those of palladium.[10]

The author is indebted to Dr. E. Challen for microanalytical determinations of carbon, hydrogen, and nitrogen, and to Mr. I. Reece for the spectrophotometric measurements in nitrobenzene.

Department of Inorganic Chemistry, N.S.W. University of Technology,
Broadway, Sydney, Australia. [*Received, July 15th*, 1958.]

[7] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127; Harris and Nyholm, *J.*, 1956, 4375—4383.
[8] Elliot and Pauling, *J. Amer. Chem. Soc.*, 1938, **60**, 1846.
[9] Harris and Reece, *Nature*, in the press.
[10] Harris, Livingstone, and Reece, *Austral. J. Chem.*, 1957, **10**, No. 3, 282—286.

137. *Studies in Stereochemical Structure. Part XII.* The Resolution of (±)-Atrolactamidinium Chloride.*

By R. Roger and D. G. Neilson.

(±)-Atrolactamidinium chloride has been prepared from acetophenone cyanohydrin *via* ethyl (±)-atrolactimidate hydrochloride. (±)-Atrolactamidine was resolved by separation of the diastereoisomeric salts with optical active mandelic acid. (−)-Atrolactic acid, isolated from (−)-atrolactamidinium chloride, was of at least 90% optical purity.

The amidines have been studied extensively;[1] few optically active amidines, however, have been described, although Cohen and Marshall[2] prepared and unsuccessfully attempted to resolve *N*-(−)-bornyl-*N'*-(+)-bornylbenzamidine with (+)-camphorsulphonic acid. The amidinium ion (I) so formed, however, is now known to be a *meso*-form[1] and hence cannot be resolved. Cohen and Marshall[2] also prepared substituted benzamidines [II; R = (−)-menthyl, R' = Me, Et, and Ph] but in these the optically-active centres were constituents of the functional amidine groups.

(I) $[C_{10}H_{17}\cdot NH{=}CPh{=}NH\cdot C_{10}H_{17}]^+$ $\qquad$ $R'\cdot NH\cdot CPh{:}NR$ (II)

In an attempt to prepare amidines with a permanent centre of asymmetry external to, and separate from the amidine system, Roger and Reid[3] synthesised (−)-mandelamidinium chloride from amygdalin. They also resolved (±)-mandelamidine by means of (+)-camphorsulphonic acid and (+)-bromocamphorsulphonic acid. The following resolution, with optically active mandelic acid,[4] was undertaken to obtain other optically-active amidines.

Acetophenone cyanohydrin,[5] which could be distilled *in vacuo* in the presence of iodine as stabiliser,[6] was converted by the action of ethanol and anhydrous hydrogen chloride[7] into ethyl (±)-atrolactimidate hydrochloride (III). This was treated with alcoholic ammonia[7] to give (±)-atrolactamidinium chloride (IV), from which the base was obtained by use of aqueous alkali.

(±)-Atrolactamidinium chloride and sodium (+)-mandelate in water yielded (−)-atrolactamidine (+)-mandelate (V) of about 90% optical purity. (−)-Atrolactamidine (+)-mandelate and its stereoisomer were synthesised also by direct reaction of (±)-atrolactamidine and (+)- and (−)-mandelic acid, respectively.

Treatment of an ethereal suspension of (−)-atrolactamidine (+)-mandelate with dry hydrogen chloride yielded (−)-atrolactamidinium chloride (VI) which then was heated with aqueous sodium hydroxide. According to McKenzie's racemisation rule[8-10] (cf. also Rothe[11]), no racemisation of the atrolactic system is possible with alkali, and on acidification of the solution, (−)-atrolactic acid (VII) was isolated.

Whilst (±)-atrolactamidine was readily prepared from its hydrochloride and was quite stable, all attempts to prepare the (+)- and (−)-bases from the corresponding optically active hydrochlorides failed.

The rotatory powers of the optically-active atrolactamidinium chlorides at three

* Part XI, *J.*, 1954, 3453.

[1] See Shriner and Neumann, *Chem. Reviews*, 1944, **35**, 351.
[2] Cohen and Marshall, *J.*, 1910, **97**, 328.
[3] Roger and Reid, Ph.D. Thesis, University of St. Andrews, 1949.
[4] Roger, *J.*, 1935, 1544.
[5] Eliel and Freeman, *Org. Synth.*, 1953, **33**, 7.
[6] Hansley, U.S.P. 2,416,624 (*Chem. Abs.*, 1947, **41**, 3483).
[7] Pinner, "Die Imidoäther und ihre Derivate," Berlin, 1892.
[8] McKenzie and Wren, *J.*, 1919, **115**, 602.
[9] McKenzie and Smith, *J.*, 1922, **121**, 1348.
[10] *Idem*, *Ber.*, 1925, **58**, 894.
[11] Rothe, *Ber.*, 1914, **47**, 843.

wavelengths in the visible spectrum gave approximately straight line Lowry–Dickson plots but the determinations were not sufficient to warrant discussion; this aspect is being studied further.

$$\underset{\text{(III)}}{HO\cdot CPhMe\cdot C(OEt){:}NH_2Cl} \longrightarrow \underset{\text{(IV)}}{HO\cdot CPhMe\cdot C(NH_2){:}NH_2Cl} \longrightarrow \underset{\text{(V)}}{(-)\text{-}HO\cdot CPhMe\cdot C(NH_2){:}NH,HO\cdot CHPh\cdot CO_2H\text{-}(+)}$$

$$\underset{\text{(VI)}}{(-)\text{-}HO\cdot CPhMe\cdot C(NH_2){:}NH_2Cl} \longrightarrow \underset{\text{(VII)}}{(-)\text{-}HO\cdot CPhMe\cdot CO_2H}$$

Experimental

All specific rotations were measured in a 2-dm. tube unless otherwise stated.

Optically-active Mandelic Acids.—These were prepared by resolution of (±)-mandelic acid by Roger's method.[4]

Acetophenone Cyanohydrin.—As in the literature,[5] acetophenone (120 g.) in ether (90 ml.) was added to a solution of freshly ground sodium cyanide (123 g.) in water (150 ml.). The mixture was stirred well, and maintained at 5° during the addition of concentrated hydrochloric acid (210 ml.). The addition required two hours and stirring was continued for a further two hours at room temperature. The ether layer was separated and the aqueous layer again extracted with ether. The crude product could be distilled in the presence of iodine [6] (1 g.) yielding acetophenone cyanohydrin (48 g. from 120 g. of acetophenone), b. p. 147—149°/18 mm., as a pale yellow oil.

Ethyl (±)-Atrolactimidate Hydrochloride.—Moisture was excluded during this experiment. Acetophenone cyanohydrin (48 g.) and anhydrous ethanol (16 g.) were treated at 0° with dry hydrogen chloride (13·2 g.). After 48 hours in the ice-chest the mixture was treated with anhydrous ether, furnishing *ethyl (±)-atrolactimidate hydrochloride* (60 g.), m. p. 101—102° (decomp.) (Found: Cl^-, 15·3. $C_{11}H_{16}O_2NCl$ requires Cl^-, 15·5%).

Ethyl (±)-Atrolactimidate.—The imidate hydrochloride (5 g.) was treated with 4N-sodium hydroxide (12 ml.). The dried ethereal extract afforded *ethyl (±)-atrolactimidate* (2 g.), m. p. 56—57° [from petroleum (b. p. 60—80°)] (Found: N, 7·05. $C_{11}H_{15}O_2N$ requires N, 7·2%).

(±)-Atrolactamidinium Chloride.—An anhydrous solution of ammonia (8·5 g.) in ethanol (100 ml.) was shaken with ethyl (±)-atrolactimidate hydrochloride (23 g.) for 12 hr., and the solvent then evaporated at room temperature. The resultant solid on crystallisation from dilute hydrochloric acid gave *(±)-atrolactamidine hydrochloride* (17 g.), m. p. 174—175° after softening at 171° (Found: C, 53·6; H, 6·3; N, 14·7. $C_9H_{13}ON_2Cl$ requires C, 53·9; H, 6·5; N, 14·0%).

(±)-Atrolactamidine.—(±)-Atrolactamidinium chloride (6 g.) was shaken with 10N-sodium hydroxide (15 ml.) at 0° until a clear solution resulted. Addition of water, dropwise, afforded a flocculent precipitate which was washed with water and recrystallised from acetone. (±)-Atrolactamidine (3·7 g.) had m. p. 77—78° (decomp.). Samples of a picrate prepared (*a*) from the amidine base and (*b*) from the hydrochloride, both had m. p. 188—189°.

(±)-Atrolactamidine (±)-Mandelate.—(±)-Atrolactamidinium chloride (2·5 g.) was heated with sodium (±)-mandelate (2·2 g.) in water until a clear solution resulted. The crystals which separated on cooling were twice recrystallised from water to give *(±)-atrolactamidine (±)-mandelate* (1 g.) which softened at 152° and had m. p. 155—156° (Found: C, 64·3; H, 6·4; N, 8·2. $C_{17}H_{20}O_4N_2$ requires C, 64·6; H, 6·3; N, 8·8%).

(−)-Atrolactamidine (+)-Mandelate.—Method A. (±)-Atrolactamidinium chloride (6·7 g.) and sodium (+)-mandelate (5·8 g.), $[\alpha]_{5461}$ +123° (in water), were heated in water (37 ml.). Crystals which separated when the solution cooled were recrystallised twice from water (in each case the crystallisations were allowed to proceed undisturbed otherwise crystals of low optical purity were obtained). There resulted large rhombic crystals of (−)-atrolactamidine (+)-mandelate (2 g.) which softened at 162° and had m. p. 165° (decomp.), $[\alpha]_{5461}^{15}$ +12·1° (*c* 0·91 in methanol).

Method B. Ethereal (+)-mandelic acid (1·5 g.), $[\alpha]_{5461}$ +186° (in acetone), was mixed with (±)-atrolactamidine (1·6 g.) dissolved in alcohol, the amidine salt being precipitated. *(−)-Atrolactamidine (+)-mandelate* (0·7 g.), with m. p. as above, had $[\alpha]_{5461}$ + 15·6° (*c* 0·86

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in methanol) after two recrystallisations from water (Found: C, 64·8; H, 6·0. $C_{17}H_{20}O_4N_2$ requires C, 64·6; H, 6·3%).

(+)-*Atrolactamidine* (−)-*Mandelate*.—This salt was prepared as in method B, but with (−)-mandelic acid, $[\alpha]_{5461}$ −188° (in acetone). After being twice recrystallised from water, (+)-*atrolactamidine* (−)-*mandelate* softened at 162°, melted at 165° (decomp.), and had $[\alpha]^{16}_{5416}$ −13·5° (*c* 0·86 in methanol) (Found: C, 65·2; H, 6·6; N, 9·3%).

(−)-*Atrolactamidinium Chloride*.—(−)-Atrolactamidine (+)-mandelate, $[\alpha]_{5461}$ +12·4° (in methanol), was set aside with an anhydrous ether solution of hydrogen chloride for 24 hr. The amidinium chloride was filtered off, dissolved in warm ethanol, cooled, and reprecipitated with ether. (−)-*Atrolactamidinium chloride*, m. p. 200—201° (decomp.) after softening at 197°, had $[\alpha]^{15}_{5461}$ −55·6° (*c* 0·54 in water) (Found: C, 54·1; H, 6·4; N, 13·2. $C_9H_{13}N_2OCl$ requires C, 53·9; H, 6·5; N, 14·0%).

(+)-*Atrolactamidinium Chloride*.—Similarly, (+)-atrolactamidine (−)-mandelate, $[\alpha]_{5461}$ −13·5° (in methanol), yielded (+)-*atrolactamidinium chloride*, which softened at 197°, melted at 201° (decomp.), and had $[\alpha]^{15}_{5461}$ +54·8° (*c* 0·58 in water). The yield was almost theoretical.

Optical Rotations $[\alpha]^{15}_{\lambda}$ *(in Water) of the Optically-active Hydrochlorides*.—

λ (Å)	6234	5780	5461
(−)-Atrolactamidinium chloride (*c* 0·54)	−42·9°	−51·9°	−55·6°
(+)-Atrolactamidinium chloride (*c* 0·58)	+43·7°	+49·7°	+54·8°

(−)-*Atrolactic Acid*.—(−)-Atrolactamidinium chloride (0·5 g.), $[\alpha]_{5461}$ −54·7° (in water), was heated in 4N-sodium hydroxide until evolution of ammonia ceased. The acidified solution, on extraction with ether, yielded (−)-atrolactic acid (0·2 g.) which was crystallised from benzene (charcoal), and did not depress the m. p. of authentic acid. It had $[\alpha]_D^{22}$ −48·3° (*c* 0·55 in water); McKenzie and Clough [12] record $[\alpha]_D^{14}$ −53·8° (in water).

(+)- *and* (−)-*Atrolactamidines*.—Treatment of (+)- and (−)-atrolactamidinium chloride at 0° with alkali solutions of varying strengths did not give crystalline products.

One of us (D. G. N.) is indebted to the University of St. Andrews for a Post Graduate Scholarship.

Queen's College, Dundee,
University of St. Andrews. [*Received, August 21st*, 1958.]

[12] McKenzie and Clough, *J.*, 1910, **97**, 1016.

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138. *The Trialkylsilyl Esters of Boron.*

By E. W. Abel and Apar Singh.

The tristrialkylsilyl borates, $[(R_3Si{\cdot}O)_3B]$, have been obtained in good yield by a number of methods, and their thermal stability and ease of hydrolysis investigated. Bistriethylsilyl phenylboronate $[(Et_3Si{\cdot}O)_2B{\cdot}Ph]$ and triethylsilyl diphenyborinate $[Et_3Si{\cdot}O{\cdot}BPh_2]$ have been prepared. The trialkylsilyl metaborates have been formed from boric oxide and the corresponding orthoborates at high temperature; they are trimeric.

Since the first report of tristrimethylsilyl borate by Krieble,[1] there has been little systematic investigation of the chemistry of the trialkylsilyl compounds of boron. The few preparative methods reported [2,3] have been peculiar to the silyl system, only one reaction [3] being related to the normal methods of preparing organic borates. We have now prepared the trialkylsilyl borates by a number of methods analogous to those used for the alkyl borates.[4]

[1] Krieble, U.S.P. 2,440,101/1946.
[2] Voronkov and Zgonnik, *Zhur. obshchei Khim.*, 1957, **27**, 1476.
[3] Wiberg and Krüerke, *Z. Naturforsch.*, 1953, **8**, *b*, 608.
[4] Lappert, *Chem. Rev.*, 1956, **56**, 959.

Triethylsilanol and boric acid gave tristriethylsilyl borate in good yield, $3Et_3Si{\cdot}OH + H_3BO_3 \longrightarrow (Et_3Si{\cdot}O)_3B + 3H_2O$, the water being continuously removed as the benzene–water azeotrope. This reaction is much simpler than the analogous reaction leading to tertiary alkyl borates.[4] We found the reported [2] action of silanols on trialkyl borates to give only moderate yields of silyl borate, but good yields were obtained in the silanolysis of tristrimethylsilyl borate to tristriethylsilyl borate with triethylsilanol, $(Me_3Si{\cdot}O)_3B + 3Et_3Si{\cdot}OH \longrightarrow (Et_3Si{\cdot}O)_3B + 3Me_3Si{\cdot}OH$.

The preparation of alkyl borates from boron trichloride, alcohols, and pyridine has given [5] excellent yields, but the corresponding reaction with triethylsilanol gave a poor yield (34%) of the silyl borate; considerable amounts of boron trichloride–pyridine and hexaethyldisiloxane were isolated as by-products. Boron trichloride and sodium triethylsiloxide, however, afforded a good yield (73%) of the pure borate: $BCl_3 + 3Et_3Si{\cdot}ONa \longrightarrow 3NaCl + (Et_3Si{\cdot}O)_3B$. Sodium triethylsiloxide also gave bistriethylsilyl phenylboronate, $Ph{\cdot}B(O{\cdot}SiEt_3)_2$, and triethylsilyl diphenylborinate, $Ph_2B{\cdot}O{\cdot}SiEt_3$, from phenylboron dichloride and diphenylboron chloride, respectively.

The most convenient preparation of tristrialkylsilyl borates was the silanolysis of trisdiethylaminoboron: [6] $3Et_3Si{\cdot}OH + (Et_2N)_3B \longrightarrow (Et_3Si{\cdot}O)_3B + 3Et_2NH$. The reaction required no solvent, and removal of diethylamine at reduced pressure gave the pure borate, which distilled unchanged.

Phenylboronic anhydride did not react with hexamethyldisiloxane as did boric oxide [2] to form an ester. Boric oxide, however, caused fission of ethoxytrimethylsilane to give a mixture of triethyl and tristrimethylsilyl borates, which are easily separated by distillation: $3EtO{\cdot}SiMe_3 + B_2O_3 \longrightarrow (EtO)_3B + (Me_3Si{\cdot}O)_3B$.

The tristrialkylsilyl borates are not hydrolysed rapidly, more than 50% being recovered after being shaken with water for long periods. This slow hydrolysis is presumably due to considerable steric hindrance by the three large trialkylsilyl groups. This steric effect on the rate of hydrolysis of borates has been extensively investigated.[7] The lower steric hindrance in the phenylboron esters explains the faster hydrolysis of these compounds than of the borates. The resistance of trialkylsilylboron esters to hydrolysis may be further enhanced by the powerful water-repelling properties of the silanols and disiloxanes formed on hydrolysis.

Hydrogen chloride and bromide reacted rapidly and completely with tristrimethylsilyl borate to produce boric acid and the corresponding trimethylhalogenosilanes: in this the borate closely resembles the tertiary alkyl esters of boron.[8]

Reaction of boric oxide with the tristrialkylsilyl borates produced the trialkylsilyl metaborates: $(R_3Si{\cdot}O)_3B + B_2O_3 \longrightarrow (R_3Si{\cdot}O{\cdot}BO)_3$. These compounds are trimeric like the corresponding alkyl metaborates,[9,10] and we believe them to have the cyclic boroxole structure [11] of the alkyl metaborates. This is supported by the presence of the doublet band at 720 and 735 $cm.^{-1}$ in the infrared spectrum, which has recently been assigned [10] to the out-of-plane vibrations of the boroxole skeleton. It is to be noted that tertiary alkyl metaborates of similar structure do not exist. Whereas the tristrialkylsilyl borates can be refluxed unchanged, the silyl metaborates decompose on attempted distillation to boric oxide and the corresponding orthoborate. The metaborates can, however, be heated for 50 hr. in a sealed tube at 250° without decomposition; the orthoborates have been recovered unchanged after being heated in sealed tubes at 275°.

The strongest bands in the infrared spectrum of all the compounds reported above are

[5] Lappert, *J.*, 1953, 667.
[6] Gerrard, Lappert, and Pearce, *J.*, 1957, 381.
[7] Steinburg and Hunter, *Ind. Eng. Chem.*, 1957, **49**, 174.
[8] Gerrard and Lappert, *J.*, 1951, 2545.
[9] Goubeau and Keller, *Z. anorg. Chem.*, 1951, **267**, 1.
[10] Lappert, *J.*, 1958, 2790.
[11] Goubeau and Keller, *Z. anorg. Chem.*, 1953, **272**, 303.

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due to the B–O stretching modes [12,13] in the 1300—1400 cm.$^{-1}$ region, with a maximum absorption at 1334 ± 5 cm.$^{-1}$, except in the metaborates where the maximum occurs at 1380 cm.$^{-1}$.

Experimental

Analyses and molecular-weight measurements were made by the Microanalytical Laboratory, Imperial College.

Preparations.—Triethylsilanol,[14] ethoxytrimethylsilane,[15] trisdiethylaminoboron,[6] phenylboron dichloride,[16] and diphenylboron chloride [16] were prepared by established methods. Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrometer with sodium chloride optics.

Interaction of Boric Acid and Triethylsilanol.—The acid (0·51 g., 1 mol.), triethylsilanol (5·32 g., 5 mol.), and benzene (20 ml.) were heated slowly, and the water–benzene azeotrope allowed to distil off (2 hr.). Careful fractionation of the residue gave hexaethyldisiloxane (1·38 g.), b. p. 60°/1 mm., n_D^{20} 1·4340, and tristriethylsilyl borate (2·94 g., 89% on H_3BO_3 taken), b. p. 120°/1 mm., n_D^{20} 1·4370 (Found: B, 2·68. Calc. for $C_{18}H_{45}O_3BSi_3$: B, 2·73%).

Silanolysis Reactions.—(a) *Triethylborate with triethylsilanol.* The borate (1·60 g., 1 mol.) and silanol (4·32 g., 3 mol.) were slowly fractionated (3 hr.) to yield ethanol (1·19 g., 77%), b. p. 75—80°, n_D^{20} 1·3640. Distillation of the residue produced bistriethylsilyl ether (2·03 g.), b. p. 120°/25 mm., n_D^{20} 1·4260, and tristriethylsilyl borate (1·67 g., 38%), b. p. 184°/20 mm., n_D^{20} 1·4370 (Found: B, 2·74%).

(b) *Tristrimethylsilyl borate with triethylsilanol.* The borate (2·94 g., 1 mol.) and the silanol were kept at 150° and trimethylsilanol was allowed to distil off; this underwent rapid change to bistrimethylsilyl ether (2·38 g., 91·2%), b. p. 100°, n_D^{20} 1·3779, and water (0·25 g., 80%). Distillation of the residual liquid gave tristriethylsilyl borate (3·60 g., 85%), b. p. 184°/20 mm., n_D^{20} 1·4370 (Found: B, 2·71%).

Interaction of Boron Trichloride (1 mol.) and Triethylsilanol (3 mol.) in the Presence of Pyridine (3 mol.).—The chloride (3·46 g.) in light petroleum (15 c.c.) was added (30 min.) to the silanol (11·65 g.) and pyridine (6·97 g.) in light petroleum (30 c.c.) at −80°, with constant shaking. After 24 hr. at 20°, the precipitate was filtered off and washed with light petroleum, and excess of solvent removed (20°/0·5 mm.). Pyridinium chloride (2·35 g.) was washed from the precipitate with water (3 × 20 c.c.) to leave (after being dried at 20°/0·01 mm.) pyridine–boron trichloride (3·70 g.), m. p. 114° (Found: N, 7·3%. Calc. for C_5H_5N,BCl_3: N, 7·1%). Removal of solvent from the filtrate (0°/20 mm.) and subsequent distillation gave a forerun (7·0 g.) (unchanged pyridine and hexaethyldisiloxane) and then tristriethylsilylborate (4·0 g., 34%), b. p. 185°/20 mm., n_D^{20} 1·4378 (Found: B, 2·72%).

Interaction of Sodium Triethylsiloxide and Boron Trichloride.—The siloxide (from 6·18 g. of silanol and 1·10 g. of sodium) in light petroleum (30 c.c.) was treated with boron trichloride (1·84 g.) in light petroleum (10 c.c.) at −70°. After being warmed to 20° the mixture was set aside (2 hr.), and sodium chloride filtered off. Removal of solvent from the filtrate (20°/0·1 mm.) and subsequent distillation of the residue gave tristriethylsilyl borate (4·62 g., 73%), b. p. 183°/17 mm., n_D^{20} 1·4370 (Found: B, 2·69%).

Interaction of Diphenylboron Chloride and Sodium Triethylsiloxide.—The chloride (6·45 g., 1 mol.) in benzene (20 c.c.) was added with constant shaking to sodium triethylsiloxide (4·96 g., 1 mol.) in benzene (25 c.c.), heat was evolved during addition (15 min.), and shaking was continued for 2 hr. Removal of benzene (20°/20 mm.), and subsequent distillation gave *triethylsilyl diphenylborinate* (9·20 g., 97%), b. p. 135°/0·5 mm., d_4^{20} 0·974, n_D^{20} 1·5270 (Found: C, 72·7; H, 8·3; B, 3·6. $C_{18}H_{25}OBSi$ requires C, 73·0; H, 8·8; B, 3·7%).

Interaction of Phenylboron Dichloride and Sodium Triethylsiloxide.—In the same manner we obtained *bistriethylsilyl phenylboronate* (6·30 g., 56%), b. p. 120°/0·2 mm., d_4^{20} 0·928, n_D^{20} 1·4730 (Found: C, 62·0; H, 10·4; B, 3·2. $C_{18}H_{35}O_2BSi_2$ requires C, 61·7; H, 10·0; B, 3·1%).

[12] Webster and O'Brien, *Austral. J. Chem.*, 1955, **8**, 355.
[13] Bellamy, Gerrard, Lappert, and Williams, *J.*, 1958, 2412.
[14] Di Giorgio, Strong, Sommer, and Whitmore, *J. Amer. Chem. Soc.*, 1946, **68**, 1380.
[15] Sauer, *ibid.*, 1944, **66**, 1707.
[16] Abel, Dandegaonker, Gerrard, and Lappert, *J.*, 1956, 4697.

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Interaction of Trisdiethylaminoboron and Triethylsilanol.—Triethylsilanol (4·46 g., 3 mol.) was added to trisdiethylaminoboron (2·56 g., 1 mol.); during the addition heat was evolved, and the vessel was kept at 0°. After 30 min., diethylamine (1·84 g., 75%), b. p. 55°, n_D^{20} 1·3860, was removed (20°/15 mm.). The remaining tristriethylsilyl borate (4·45 g., 98%), b. p. 182°/15 mm., n_D^{20} 1·4370 (Found: B, 2·70%), distilled unchanged (n_D^{20} 1·4371).

Attempted Fission of Hexamethyldisiloxane with Phenylboronic Anhydride.—After the compounds had been heated in a sealed tube at 250° (40 hr.) and then cooled, the siloxane (96%) and anhydride (94%) were recovered unchanged.

Interaction of Boric Oxide and Ethoxytrimethylsilane.—The silane (18·67 g.) was refluxed (5 hr.) with boric oxide (7·40 g.). After removal of unchanged boric oxide by filtration, distillation gave triethyl borate (7·87 g., 99%), b. p. 118—120°, n_D^{20} 1·3741 (Found: B, 7·3. Calc. for $C_6H_{15}O_3B$: B, 7·4%), and tristrimethylsilyl borate (11·0 g., 75%), b. p. 186°, n_D^{20} 1·3840 (Found: B, 3·97%. Calc. for $C_9H_{27}O_3BSi_3$: B, 3·89%); a glass-like residue (3·83 g.) remained.

Hydrolysis of Tristrimethylsilyl Borate.—The borate (4·5 g., 1 mol.) was shaken violently (2 hr.) with water (3·0 g., >10 mol.), and the mixture then extracted with ether. Unchanged tristrimethylsilyl borate (2·74 g., 61%), b. p. 84°/20 mm., n_D^{20} 1·3680 (Found: B, 3·8%), was obtained. After similar treatment tristriethylsilyl borate (67%) was also recovered.

Action of Hydrogen Halides on Tristrimethylsilyl Borate.—(a) *Hydrogen chloride.* The gas was passed through the ester in a very slow stream at 0°. There was an immediate evolution of heat and the products set to a solid white mass. Passage of the gas was continued for a further 10 min., then volatile matter was removed (20°/20 mm.). The residue was boric acid (0·497 g., 98%) (Found: B, 17·6. Calc. for H_3BO_3: B, 17·7%). Distillation of the condensate gave trimethylchlorosilane (2·47 g., 95%), b. p. 57°, n_D^{22} 1·3874 (Found: Cl, 31·9. Calc. for C_3H_9ClSi: Cl, 32·7%).

(b) *Hydrogen bromide.* In a similar manner we obtained boric acid (0·768 g., 88%) (Found: B, 17·9%), and trimethylbromosilane (6·28 g., 98%), b. p. 81°, n_D^{19} 1·4132 (Found: Br, 51·7. Calc. for C_3H_9BrSi: Br, 52·3%).

Formation of the Silyl Metaborates.—(a) *Trimethylsilyl metaborate.* Tristrimethylsilyl borate (5·16 g., 1 mol.) and boric oxide (1·41 g., 1·1 mol.) were heated (30 hr.) in a sealed tube at 225°. Only small traces of solid boric oxide then remained, and the mixture was poured into ether (20 c.c.) and stored (24 hr.) in a stoppered flask. After filtration, solvent was removed (20°/0·1 mm.) to leave *trimethylsilyl metaborate* (5·63 g., 87%), d_4^{20} 0·988, n_D^{20} 1·4101 (Found: C, 30·4; H, 7·4; B, 9·5%; *M*, 331. $C_9H_{27}O_6B_3Si_3$ requires C, 31·0; H, 7·8; B, 9·3%; *M*, 348), as a slightly viscous liquid.

(b) *Triethylsilyl metaborate.* Tristriethylsilyl borate and boric oxide reacted as described in (a) to produce *triethylsilyl metaborate* (7·65 g., 84%), d_4^{20} 0·955, n_D^{20} 1·4360 (Found: C, 46·2; H, 8·9; B, 6·9%; *M*, 450. $C_{18}H_{45}O_6B_3Si_3$ requires C, 45·5; H, 9·5; B, 6·8%; *M*, 474).

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139. *The Production of Active Solids by Thermal Decomposition. Part X.* Heat Treatment of the Xerogels of Silica.*

By J. F. Goodman and S. J. Gregg.

Ion-free silica gel was prepared by the hydrolysis of silicon ethoxide, and separate portions were calcined at a series of fixed temperatures from 200° to 1460° c. Sorption isotherms of nitrogen, carbon tetrachloride, and methanol were then measured on the cooled product, its density was determined by immersion in three liquids (including mercury), and it was examined by *X*-ray and electron diffraction and by electron microscopy.

The average pore size remains almost constant from 200° to 900°, though both the specific surface and the pore volume (and with it the lump volume) diminish markedly; the loss of surface and of pore volume begins to accelerate in the region of the Tammann temperature (about 790° c). The sintering behaviour of silica, which is in marked contrast to that of, *e.g.*, ferric oxide, is due to the amorphous nature of silica, which persisted to *ca.* 1400°.

The curve of specific surface against temperature of calcination of hydrous oxides is likely to show a continuous decline as temperature increases, if no new phase is produced when the water is driven off.[1] Silica gel is an oxide of a different kind from those previously considered, for (except after high-temperature treatment) it is amorphous, *i.e.*, it possesses only short-range order. Correspondingly the effect of heat on both surface area and pore structure shows interesting differences from that encountered with crystalline solids.

Experimental

Materials.—Ion-free silica gel was prepared by hydrolysis of silicon ethoxide by a method similar to that of Weiser, Milligan, and Coppac.[2] The ester in alcohol was poured, with stirring, into an excess of distilled water. Stirring was continued for 4 days, then the mixture was kept at room temperature for 3 months, after which a copious white gel had separated. This was filtered off at the pump and thoroughly washed with absolute alcohol by decantation to remove undecomposed ester. After filtration the solid was stirred with 2 l. of distilled water, and left for two weeks. Finally, the gel was spread out, air-dried at 25°, and broken into lumps.

On thermogravimetric analysis with the temperature of the furnace rising at 200° per hour, the product lost weight rapidly up to a furnace temperature of *ca.* 200°, then more slowly to much higher temperatures. There was no evidence for a stoicheiometric hydrate and the results are consistent with the loss of water from a hydrous oxide.

Procedure.—Portions of the gels were heated for 5 hr. at a fixed temperature in the range 200—1460° on the thermal balance, and the properties of portions of the cooled product were examined as follows: (i) the specific surface by sorption of nitrogen at −183° volumetrically; [1b] (ii) the sorption isotherm at 22° of the vapour of carbon tetrachloride and of methanol, with the electromagnetic sorption balance; [3] (iii) the apparent density by immersion in mercury,[4] carbon tetrachloride, or water [5] (ρ_{Hg}, ρ_{CCl_4}, ρ_{H_2O}); (iv) (for selected samples) the *X*-ray powder photograph, the selected area diffraction pattern, and the electron micrograph; the electron optical examination was carried out with a Siemens Elmiskope I operated at 80 kv; portions of the solid were crushed and suspended in alcohol, a drop of this suspension being dried on a grid covered with a carbon film.

The water content w corresponding to each temperature of calcination was obtained by

* Part IX, *J.*, 1956, 3612.

[1] (*a*) Gregg, *J.*, 1953, 3940; (*b*) Gregg and Stevens, *J.*, 1953, 3951.
[2] Weiser, Milligan, and Coppac, *J. Phys. Chem.*, 1939, **43**, 1109.
[3] Gregg, *J.*, 1955, 1438.
[4] Goodman and Gregg, *J.*, 1956, 3612.
[5] Cf. Culbertson and Dunbar, *J. Amer. Chem. Soc.*, 1937, **59**, 306.

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repeating the calcination with a separate portion of the starting material, and then raising the temperature to 1000° until constant weight was obtained as registered on the thermal balance.

In addition, a portion of the starting material of each batch was examined dilatometrically: the solid was made into a paste with water, and then compacted by compression in a die (0·375 in. diam.) at 2000 lb./sq. in. by a hydraulic press. The compact, about 3 cm. long, was subjected, in a simple extensometer [6] to a temperature rising steadily at 200° per hour, its length being read frequently.

The results for the isotherms (ii) and density (iii) led to separate estimates of the pore volume, V_I and V_D respectively. V_I could be calculated as x_s/ρ, where ρ is the density of the sorbate in the liquid form, merely by applying the Gurvitch relationship to the amount, x_s (g.), sorbed at saturation. The calculation of V_D depends on the fact that, with a pressure difference of 1 atm. across the meniscus, mercury cannot enter pores of diameter less than about 5 μ whereas the molecules of carbon tetrachloride and of water can penetrate pores with a diameter as small as *ca.* 5 Å or *ca.* 3 Å respectively. Thus the reciprocal of the density measured in mercury is the lump volume, and the differences $(1/\rho_{Hg} - 1/\rho_{H_2O})$ and $(1/\rho_{Hg} - 1/\rho_{CCl_4})$ are the volumes of pores with diameters between 5 μ and *ca.* 3 or 5 Å respectively. The calculations for both V_D and V_I are based on the assumption that the liquid or adsorbate retains its ordinary liquid density throughout the system; but if, as is probable, the density in the finest pores is higher than normal, the calculated pore volumes would be high (by perhaps a few %), and the enhancement might vary from liquid to liquid. This compression effect, combined with the further penetration of water because of its smaller molecular size, is sufficient to account for the small but not negligible difference between the pore volume measured by a given method with two different liquids (cf. Table). By combination of the values of pore volume with the

Temp.*	Colour	w †	θ ‡	ρ_{CCl_4} (g. cm.$^{-3}$)	ρ_{H_2O} (g. cm.$^{-3}$)	$10^8 V/S'$ (cm.)
25°	White	13·5	1·0	—	—	—
200	,,	6·5	0·46	2·06	2·18	6
400	,,	4·0	0·32	2·09	2·21	5·8
600	,,	1·75	0·16	2·11	2·27	6·1
800	,,	0·55	0·07	2·16	2·27	6·4
900	,,	0·2	0·04	2·13	2·27	7·4
1000	,,	0·0	0·0	2·04	2·08	137
1100	Pale brown	—	—	2·12	2·07	231
1200	,,	—	—	2·09	2·07	2200
1300	Brown	—	—	—	2·05	—
1400	,,	—	—	2·05	—	—
1460	Grey	—	—	2·31	—	—

* Temperature of calcination (5 hr.).
† Volatile matter content (g. per 100 g. of SiO_2).
‡ Fraction of surface covered with chemisorbed water (assuming 1 molecule of H_2O occupies 15 Å^2).

results of the measurement of specific surface (S') information as to pore structure is obtained. The simple volume : surface ratio V_D/S' or V_I/S' is useful; for a system of cylindrical pores of fairly uniform size V/S' is indeed equal to one half of the average pore radius, and for pores of more complicated shape, *e.g.*, the interstices between spherical particles of solids, the ratio still gives a useful approximation to an average pore width.

Discussion

Results.—A striking feature is that the specific surface S' and the pore volume V both fall at approximately the same rate over a wide range of temperature: V/S' (and the average pore width) remains constant (within a few %) from 200—900°, even though both S' and V have fallen to less than one-half (Table; Fig. 1). The lump volume falls correspondingly as does the volume of the compact in the extensometer experiments (Fig. 1). These results are similar to those found by van Nordstrand, Kreger, and Ries [7] with silica

[6] Goodman, Thesis, London University, 1955.
[7] van Nordstrand, Kreger, and Ries, *J. Phys. Chem.*, 1951, **55**, 621.

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aerogel and a silica-bead catalyst. Now at the low temperatures considered, where actual migration of units of molecular or ionic size through the solid is improbable, the loss of surface must result from the adhesion of neighbouring primary particles, amounting to the removal of a pore. And if V/S' is to remain constant, such removal must occur without upsetting the rest of the lump. The remainder of the primary particles in the lump must retain their relative positions, so that the lost pore volume is in effect transferred to the outside of the lump, as shown by the fall in lump volume. The sorption isotherms of methanol and of carbon tetrachloride (Figs. 2 and 3) support the conclusion that the pore-size distribution does not change significantly as the temperature of calcination rises: they are of the same shape throughout, and the pressure at which the hysteresis loop opens changes remarkably little with temperature for a given adsorbate.

It is noteworthy that the sample at 200° (the lowest temperature for which there are data) has a pore volume not far different from the volume of the solid material (*ca.* 0·40 cm.^{3} g.$^{-1}$ as compared with 0·49 cm.^{3} g.$^{-1}$, carbon tetrachloride data being used). Thus the holes are of about the same size, shape, and number as the solid primary particles. The simplest model for this is of lumps of material made up of roughly cubic primary particles (of side *ca.* 50 Å), the holes corresponding to missing cubes. The loss of pore volume and surface up to 900° would then consist largely in local shifts of primary particles into neighbouring vacancies, which could occur without greatly upsetting the remainder of the lump if the bridges between particles were flexible. The model is, of course, over-simplified. The opacity of the gel shows that there are large pores having dimensions about the wavelength of light; the isotherms show that there is a *distribution* of pore sizes, for a single size would correspond to a vertical branch in the isotherm, *i.e.*, to a single pressure. Although it is unlikely that the particles are accurate cubes, the related model of equal spheres is less probable, for when a vacancy was filled by movement of a neighbouring sphere, there would be negligible loss of surface, since the moved sphere would touch its neighbours at isolated points only; more likely is some intermediate model, such as severely flattened irregular spheres.

The electron micrographs broadly support these inferences. (*a*) and (*b*) of the Plate show typical gel fragments from samples heated at 200° and 600°. They appear very similar, and at higher magnifications particles of the correct order of magnitude can be seen within the fragments. At higher temperatures, fragments showing smooth fracture edges become progressively more predominant. In (*c*) and (*d*) the small primary particles are no longer distinguishable although holes which may be portions of sealed pores are visible. However, in other fragments from the same samples [cf. (*e*) of Plate] particles of about 50 Å are discernible, providing good evidence that the loss of pore structure from some portions of the gel does not greatly influence the rest of the lump.

An essential feature of our model is the flexibility of the bridges; these could well be hydrogen bonds between hydroxyl groups of contiguous particles. Such bonds would be weak and not strongly directed, and the joining of neighbouring particles on sintering would involve the conversion of hydrogen bonds into siloxane bonds which are directional owing to their having partial covalent character, with consequent loss of flexibility. Thus the loss of pore volume and of surface should be accompanied by loss of "water," and accordingly it is satisfactory that the water content and the calculated fraction, θ, of surface covered by hydroxyl groups progressively diminish from 200° to 900° (see Table). The electron-diffraction patterns of samples heated below *ca.* 1460° have diffuse rings characteristic of liquids and amorphous solids (*e.g.*, glasses), showing that the solid possesses only short-range order, and implying that the structural units (silica tetrahedra) are joined randomly. When siloxane bridges form between contiguous amorphous particles, the composite particles must still be amorphous, for the original disorder remains. Moreover, the composite particle will tend to contain minute pores representing vestiges of the original, larger, gaps between the primary particles [(*c*) and (*d*), Plate].

Above *ca.* 700° the rate of loss of both pore volume and specific surface with rising

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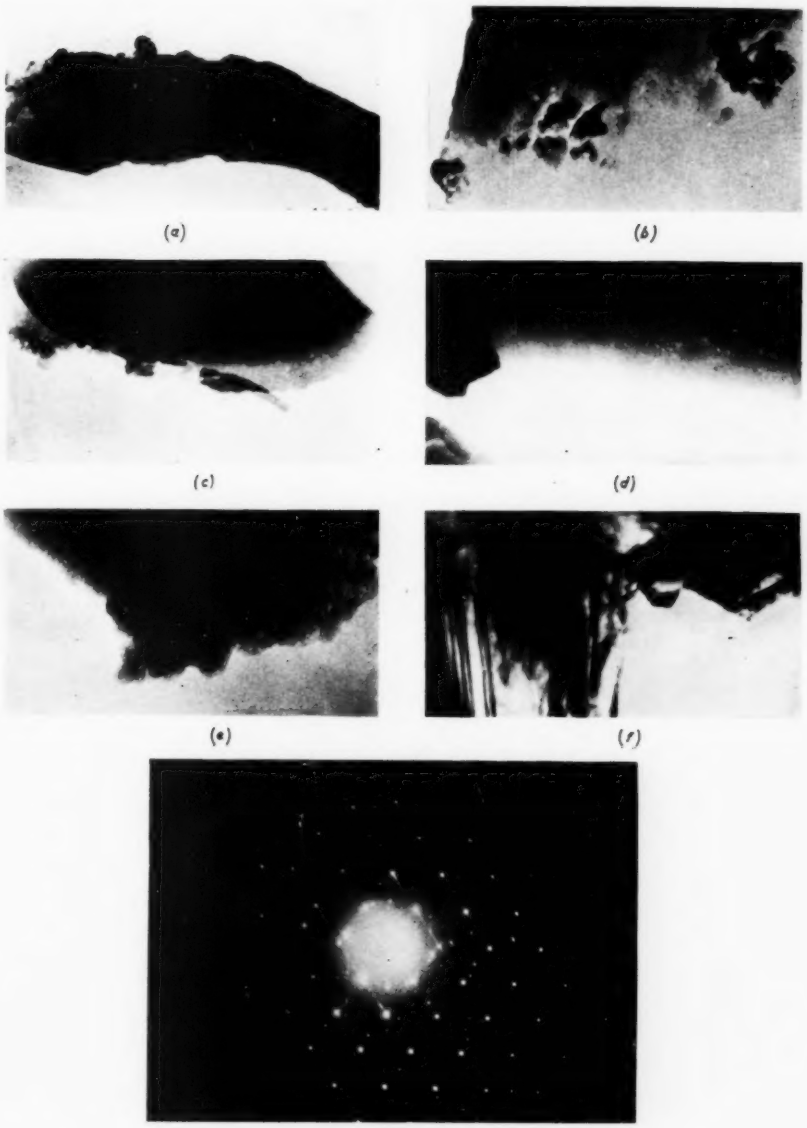
PLATE. *Electron micrographs (a to f) and electron diffraction pattern (g) of silica gel heated for five hours. The temperature of heating and the magnification are noted.*



(a) 200° (×51,000)
(b) 600° (×68,000)
(c) 1000° (×87,000)
(d) 1100° (×106,000)
(e) 1000° (×200,000)
(f) 1460° (×206,000)
(g) 1460°. Electron diffraction pattern of sample shown in (f)

[*To face p.* 696.

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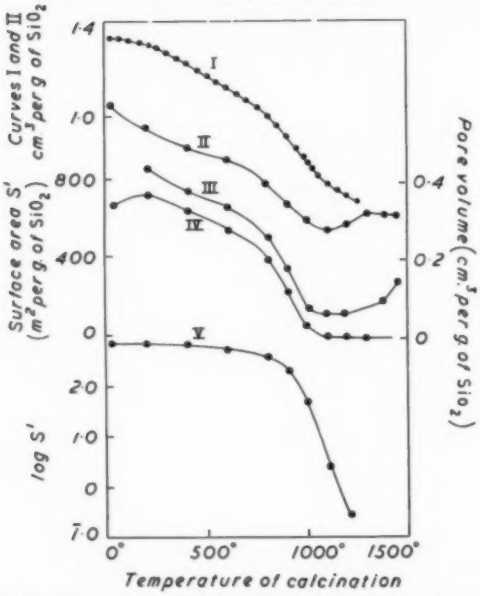
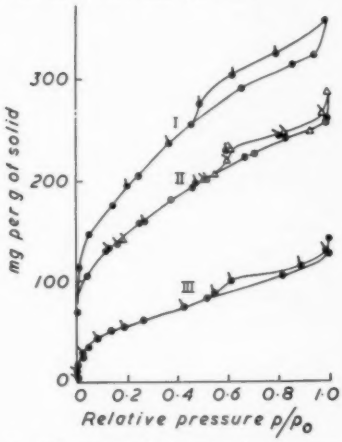
FIG. 1. *Calcination of precipitated silica.*



I, Contraction; II, lump volume; III, pore volume; IV, surface area S'; V, log S'.

For curve I the sample was compacted at 2000 lb./sq. in. and was raised in temperature at 200° per hr. For curves II—V the sample was heated at the given temperature for 5 hr.

FIG. 2. *Sorption isotherms of methanol at 22° on silica gel heated at* I, 200°; II, 600°; III, 900° *for 5 hr.*



● 1st run, ○ 2nd run, △ 3rd run. Symbols with a "tail" denote desorption.

FIG. 3. *Sorption isotherms of carbon tetrachloride. Conditions and symbols as in Fig. 2.*

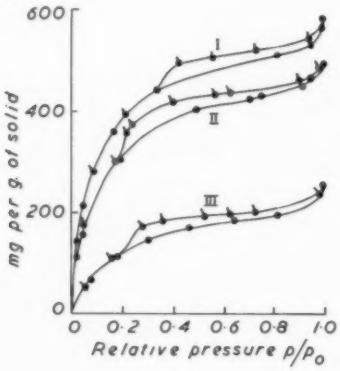
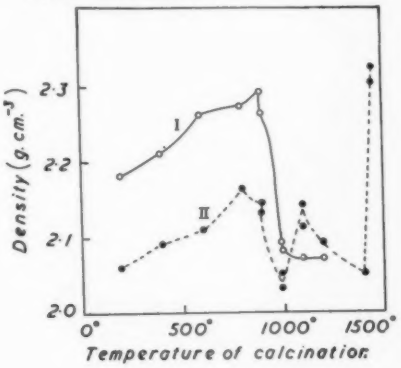


FIG. 4. *Density of precipitated silica after calcination for 5 hr., determined by* I, *water*; II, *carbon tetrachloride.*



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temperature rapidly increases (Fig. 1). Milligan and Rachford [8] found that the pore volume (measured by the uptake of water at saturation) of a commercial silica gel began to fall rapidly at 790° and by 900° was less than one tenth of its value at 600°. van Nordstrand, Kreger, and Ries [7] found similar behaviour with a silica xerogel. Below *ca.* 1460° the gel is amorphous like a glass, and the temperature at which sintering accelerates can probably be identified with the well-known tranformation temperature [7] between the supercooled liquid and glassy states. At room temperature the viscosity (η) of glass is *ca.* 10^{20} poises so that viscous flow is almost undetectable, and the material behaves as an elastic brittle solid. At the transformation temperature the viscosity of silica is *ca.* 10^{13} poises. Since the coefficient of rigidity (n) of most solids is of the order of 10^{11} c.g.s. units, this implies that the Maxwell relaxation time (the relaxation time of stresses at constant strain, $= \eta/n$) is of the order of 100 sec. On a simple picture, then, it appears that the time of experiments has reached the time of atomic adjustments, and, consequently, the structural units have enhanced mobility. It seems likely that the enhanced sintering observed above 700° is caused by the increased mobility of the $(SiO_4)^{4-}$ tetrahedra when the Maxwell relaxation time becomes considerably less than the heating time of 5 hr.

Although the rate of sintering changes at *ca.* 700°, V/S' remains constant, showing that the qualitative *effect* of sintering remains unchanged. It seems likely that both above and below this temperature the sintering mechanism is the same and occurs by a viscous flow process; but below 700° the very high viscosity allows sintering to occur only in regions where adhesion is promoted by the conversion of hydrogen bonds into directed siloxane bonds.

Such behaviour may be contrasted to that of ferric oxide [4,10] whose specific surface is largely reduced even at low temperatures. This solid being crystalline, the adhesion and growth of junctions can occur by movement of dislocations even at low temperatures, since the crystal lattice itself is the transport medium. It is noteworthy that the accelerated loss in pore volume occurs at approximately the Tammann temperature [half the m. p. (°K)] for both silica and ferric oxide gels. With ferric oxide, however, this effect is believed to result from large-scale diffusion of ions (cf. Finch and Sinha [11]), whereas with silica it is caused by the enhanced mobility of the $(SiO_4)^{4-}$ tetrahedra due to a reduction in viscosity.

Further data indicate that in the Tammann range the viscosity is not reduced sufficiently for crystals to grow. Thus the mobility of the $(SiO_4)^{4-}$ units must be considerably restricted, at any rate up to 1400°, for both the *X*-ray and the electron-diffraction results fail to show any marked ordering below this temperature. The anomalous results for density (Fig. 4) point in the same direction: the *fall* in density within the Tammann temperature range is most readily explained in terms of a sealing off, but not complete annihilation, of pores, a process which would result from a restricted mobility. A faint crystobalite pattern was discerned in the *X*-ray powder photograph for 1400°, and the electron-diffraction patterns of the 1460° sample were highly crystalline. Individual crystals showing growth steps were isolable [(*f*), Plate] and the electron-diffraction pattern from this crystal (*g*) indicated twinning and stacking faults. We find an exactly analogous situation with glasses, where the transformation temperature lies considerably below the devitrification temperature.[9] The sharp rise in density between 1400° and 1460° corresponds with the final elimination of pores and conversion of the solid phase into crystalline crystobalite, but the intermediate rise between 1000° and 1100° determined in carbon tetrachloride is puzzling and may not be real; the considerable difference between the value measured in water and in carbon tetrachloride might denote the presence of pores

[8] Milligan and Rachford, *J. Phys. Chem.*, 1947, **51**, 333.
[9] See Jones, "Glass," London, Methuen and Co., Ltd., 1956.
[10] Gregg and Hill, *J.*, 1953, 3945.
[11] Finch and Sinha, *Proc. Roy. Soc.*, 1957, *A*, **239**, 145.

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capable of admitting only the latter and/or it could be caused by a relatively greater increase in density of water than of carbon tetrachloride at the surface of the solid. Probably both effects are present together.

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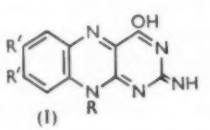
140. *Pteridine Derivatives. Part VII.* The Synthesis of Riboflavin 2-Imine and Related* iso*Alloxazine 2-Imines.*

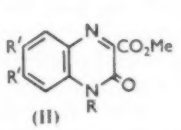
By R. M. CRESSWELL, A. C. HILL, and H. C. S. WOOD.

A new synthesis of *iso*alloxazine 2-imines (I) is described which starts from methyl 4-alkyl-3 : 4-dihydro-3-oxoquinoxaline-2-carboxylates (II) and guanidine. The 2-imine-analogue of riboflavin was synthesised by this method. Intermediate compounds formed in the reaction have been identified as octahydroglyoxaline-4-*spiro*-2′-quinoxalines (III). A second synthesis of an *iso*alloxazine 2-imino (I; R = R′ = Me) from 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine and the dimer of 3 : 4-dimethyl-*o*-benzoquinone is also described. The formation of 2-aminoalloxazines (IV) on treatment of the *iso*alloxazine 2-imines (I) with dilute alkali is discussed in relation to the fine structure of the *iso*alloxazine 2-imines.

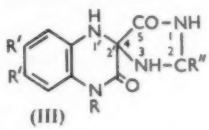
CERTAIN of the naturally occurring purines have been shown to stimulate the production of riboflavin by the mould *Eremothecium ashbyii* without at the same time affecting the growth of the organism.[1,2,3] In particular, experiments with labelled adenine indicate that the purines contribute an intact pyrimidine ring to the riboflavin molecule,[2] after loss of $C_{(8)}$. Recent views on the biosynthesis of pteridines suggest that these are also formed from purines *via* an intermediate 4 : 5-diaminopyrimidine derivative.[4] There is thus the possibility that riboflavin and the pteridines arise from some common intermediate, and it seemed to us desirable to investigate the synthesis and properties of the 2-imine of riboflavin (I; R = D-ribityl, R′ = Me) which contains the 2-amino-4-hydroxypteridine structure characteristic of most naturally occurring pteridines.



(I)



(II)



(III)

Recently two syntheses of an *iso*alloxazine 2-imine (I; R = R′ = Me) have been reported,[5,6] but in view of the low yields in these reactions together with the observation [7] that many unsuccessful attempts had been made to prepare riboflavin 2-imine, it appeared unlikely that standard *iso*alloxazine syntheses would be successful. Modification of a recent pteridine synthesis [8] seemed feasible.

* Part VI, *J.*, 1958, 3730.

[1] McNutt, *J. Biol. Chem.*, 1954, **210**, 511; Goodwin and Pendlington, *Biochem. J.*, 1954, **57**, 631.
[2] McNutt, *J. Biol. Chem.*, 1956, **219**, 365.
[3] Brown, Goodwin, and Jones, *Biochem. J.*, 1958, **68**, 40.
[4] Albert, *ibid.*, 1957, **65**, 124; Ziegler-Günder, Simon, and Wacker, *Z. Naturforsch.*, 1956, **11**b, 82.
[5] Hemmerich, Fallab, and Erlenmeyer, *Helv. Chim. Acta*, 1956, **39**, 1242.
[6] Hemmerich, *ibid.*, 1958, **41**, 514.
[7] Hitchings, Ciba Symposium on the "Chemistry and Biology of Pteridines," Churchill, London, 1954, p. 121.
[8] Dick, Fidler, and Wood, *Chem. and Ind.*, 1956, 1424.

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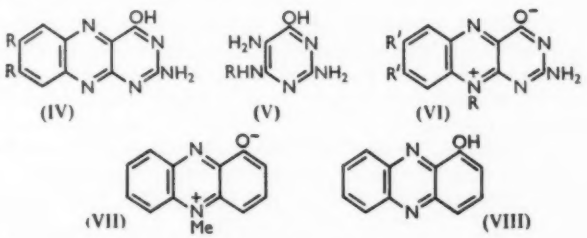
Condensing methyl 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate (II; R = Me, R′ = H), prepared by *N*-methylation of the corresponding hydroxy-ester, with guanidine gave a variety of products depending on the conditions. Fusion with guanidine carbonate, conditions which were successful for the synthesis of a pteridine derivative,[8] gave a mixture including a large proportion of guanidine 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate, and this was also obtained from the same components in refluxing aqueous methanol.

A base-catalysed condensation would formally resemble the familiar pyrimidine synthesis [9] from guanidine and β-keto-esters. However, the *N*-methyl ester with guanidine in the presence of sodium methoxide gave a high yield of 2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-octahydro-2-imino-4′-methyl-3′ : 5-dioxoglyoxaline-4-*spiro*-2′-quinoxaline (III; R = Me, R′ = H, R″ = NH). This compound had an ultraviolet absorption spectrum (Table) analogous to that of the tetrahydroquinoxaline*spiro*hydantoins described by Clark-Lewis.[10] The *N*-methyl ester with urea gave an analogous product (III; R = Me, R′ = H, R″ = O) which on methylation (methyl iodide–acetone–potassium carbonate) gave a trimethyl derivative identical with a sample prepared from 3-hydroxyquinoxaline-2-carboxyureide by Clark-Lewis's method.[10]

Ring closure to the alloxazine ring system was finally achieved by prolonged reaction of the *N*-methyl ester (II; R = Me, R′ = H) with guanidine. Unexpectedly, the product proved to be 2-amino-4-hydroxybenzo[*g*]pteridine (IV; R = H), identical with the compound prepared under similar conditions from methyl 3-hydroxyquinoxaline-2-carboxylate. The identity of these products was confirmed by comparison of the infrared spectra of the compounds and of their dimethyl and diethyl derivatives (which were prepared by the technique outlined above). Prolonged treatment of thes *piro*-compound (III; R = Me, R′ = H, R″ = NH) with sodium methoxide gave a small yield of the same benzopteridine (IV; R = H). The loss of a methyl group under these conditions is unusual, and it is shown below that this is characteristic of *iso*alloxazine 2-imines (I) when treated with alkali in the presence of air. Repetition of the reaction in an atmosphere of nitrogen gave a mixture of 2 : 10-dihydro-4-hydroxy-2-imino-10-methylbenzo[*g*]-pteridine (I; R = Me, R′ = H), and its decomposition product, the alloxazine derivative (IV; R = H). Separation of these compounds was achieved readily by paper chromatography, but the extreme instability of the *iso*alloxazine 2-imine (I; R = Me, R′ = H) made its isolation in good yield very difficult.



In the hope that riboflavin 2-imine (I; R = D-ribityl, R′ = Me) would be somewhat more stable, an analogous synthesis was carried out starting from methyl 3 : 4-dihydro-6 : 7-dimethyl-3-oxo-4-D-ribitylquinoxaline-2-carboxylate (II; R = D-ribityl, R′ = Me). This compound was prepared from the corresponding acid which is readily obtained from riboflavin by treatment with dilute sodium hydroxide.[11] This ester with guanidine in the presence of sodium propoxide gave a high yield of 2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-octahydro-2-imino-6′ : 7′-dimethyl-3′ : 5-dioxo-4′-D-ribitylglyoxaline-4-*spiro*-2′-quinoxaline (III;

[9] Jaeger, *Annalen*, 1891, **262**, 365; Wheeler and Johnson, *Amer. Chem. J.*, 1903, **29**, 496.
[10] Clark-Lewis, *J.*, 1957, 422.
[11] Surrey and Nachod, *J. Amer. Chem. Soc.*, 1951, **73**, 2337.

R = D-ribityl, R′ = Me, R″ = NH) which was isolated as the crystalline hydrochloride. More prolonged reaction in the presence of air gave 2-amino-4-hydroxy-7 : 8-dimethylbenzo[*g*]pteridine (IV; R = Me; " 2-aminolumichrome "), apparently identical with the material prepared by Bardos, Olsen, and Enkoji.[12] A similar reaction carried out under nitrogen gave a mixture of products including a large proportion of 2 : 10-dihydro-4-hydroxy-2-imino-7 : 8-dimethyl-10-D-ribitylbenzo[*g*]pteridine (I; R = D-ribityl, R′ = Me; " 2-iminoriboflavin "). Isolation of pure riboflavin 2-imine was achieved, with difficulty, by chromatography on " Florisil " columns, or alternatively by repeated precipitation from acid. These experiments were carried out in the dark as riboflavin 2-imine readily underwent photolysis.

2 : 10-Dihydro-4-hydroxy-2-imino-7 : 8 : 10-trimethylbenzo[*g*]pteridine (I; R = R′ = Me; " 2-iminolumiflavin ") could not be prepared by condensing methyl 3 : 4-dihydro-4 : 6 : 7-trimethyl-3-oxoquinoxaline-2-carboxylate (II; R = R′ = Me) with guanidine, although the intermediate *spiro*-compound (III; R = R′ = Me, R″ = NH) was formed readily in good yield. Condensing 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine [13] (V; R = Me) with the dimer of 3 : 4-dimethyl-*o*-benzoquinone,[12] however, gave the *iso*alloxazine 2-imine (I; R = R′ = Me) which was isolated as the crystalline hydrochloride. This compound had ultraviolet absorption identical with that of the material prepared by Hemmerich *et al.*[5,6] and both the free bases and the hydrochlorides showed similar R_F values on paper chromatography in several solvent systems (we are indebted to Dr. Hemmerich for these observations).

The *iso*alloxazine 2-imines (I), when treated with dilute alkali in the presence of air, readily lose the 10-alkyl substituent with the formation of 2-aminoalloxazine derivatives (IV). This behaviour is in distinct contrast with that of *iso*alloxazines such as riboflavin and lumiflavin which under similar conditions undergo ring cleavage to quinoxaline derivatives.[11,14] and it may have some bearing on the biological transfer of C_1—C_5 fragments. For *iso*alloxazines and *iso*alloxazine 2-imines (I) there is the possibility of resonance involving dipolar forms such as (VI). The insolubility of the imines in chloroform and other non-polar solvents makes it likely that the contribution of such ionic forms to the resonance hybrid is much greater than with *iso*alloxazines such as lumiflavin which readily dissolve in chloroform. The existence of such contributing structures may explain the ease with which 10-alkyl substituents may be cleaved from *iso*alloxazine 2-imines (I). The bacterial pigment, pyocyanine (VII), which has an analogous dipolar structure,[15] is similarly demethylated [16] in alkaline solution to 1-hydroxyphenazine (VIII).

Irradiation of riboflavin 2-imine (I; R = D-ribityl, R′ = Me) with ultraviolet light gave products analogous to those obtained on photolysis of riboflavin.[17] Thus in acid solution 2-aminolumichrome (IV; R = Me) was produced, and in alkaline solution a mixture of lumiflavin 2-imine (I; R = R′ = Me), 2-aminolumichrome (IV; R = Me), and a third, unidentified product.

It has been shown that guanine stimulates the production of riboflavin by *Eremothecium ashbyii* more effectively than do the other naturally occurring purines.[3] There is therefore the possibility that riboflavin 2-imine (I; R = D-ribityl, R′ = Me) may be an intermediate in the guanine–riboflavin transformation, being formed *via* the pyrimidine (V; R = D-ribosyl or D-ribityl) by condensation with 3 : 4-dimethyl-*o*-benzoquinone or its equivalent.[18] Riboflavin 2-imine, however, does not stimulate riboflavin synthesis in *Eremothecium ashbyii*, neither has it any inhibitory effect. (We are indebted to Dr. T. W. Goodwin for these results.) Deamination must therefore occur at some earlier

[12] Bardos, Olsen, and Enkoji, *J. Amer. Chem. Soc.*, 1957, **79**, 4704.
[13] Fidler and Wood, *J.*, 1957, 4157.
[14] Kuhn, Rudy, and Wagner-Jauregg, *Ber.*, 1933, **66**, 1956.
[15] Jensen and Holten, *Acta Chem. Scand.*, 1949, **3**, 1446.
[16] Wrede and Strack, *Z. physiol. Chem.*, 1928, **177**, 177.
[17] Shimizu, *J. Vitaminol.* (*Japan*), 1955, **1**, 39; *Chem. Abs.*, 1955, **49**, 12,631.
[18] Cf. Birch and Moye, *J.*, 1957, 412; 1958, 2622.

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stage in the guanine–riboflavin transformation, either prior to the opening of the iminazole ring or, as seems more likely, at the intermediate pyrimidine stage.

Compound	R_F (A)	R_F (B)	$\lambda_{max.}$ (mμ) (ε in parentheses) in H_2O at pH given	
Spiran (III)				
R = Me, R′ = H, R″ = NH	0·46	—	222(34,000), 298(4600)	pH 7
			213(?8,000), 236[b](19,000), 316(6100), 392(3200)	pH 1
R = Me, R′ = H, R″ = O	—	—	223(29,800), 300(4900) [ac]	
R = Me, R′ = Me, R″ = NH	0·60	—	226(28,000), 306(4600)	pH 13
			218(31,100), 241(21,800), 340(11,300), 410(7500)	pH 1
R = D-Ribityl, R′ = Me, R″ = NH	0·24	—	230[b](18,900), 306(4500)	pH 7
			220(31,500), 240[b](22,700), 342(11,300), 412(7200)	pH 1
Compounds (IV)				
R = H	0·46	0·14	218(28,800), 262(44,500), 333(7000), 416(9000)	pH 13
			212(27,800), 244(23,500), 263(32,900), 345(9200), 370[b](6200), 430[b](2100)	pH 1
R = Me	0·54	0·03	224(23,600), 264(43,650), 344(5500), 420(7400)	pH 13
			220(23,900), 266(27,500), 362(8200) [d]	pH 1
Compounds (I)				
R = Me, R′ = H	0·23	0·36	216(24,500), 264(29,800), 358(8200), 428(11,020)	pH 1
R = Me, R′ = Me	0·34	0·23	223(21,100), 268(25,000), 384 (9100), 443(10,300)	pH 1
R = D-Ribityl, R′ = Me	0·22	0·28	224(27,000), 270(32,100), 386(12,300), 442(14,100)	pH 1
Riboflavin	0·22	0·39	223(35,500), 267(35,500), 376(10,700), 445(11,500)	pH 1

[a] In EtOH. [b] Shoulder. [c] Clark-Lewis [10] gives $\lambda_{max.}$ 219 mμ (ε 21,300), and 300 mμ (4400). [d] Bardos *et al.*[12] give $\lambda_{max.}$ 266 (ε 38,900) and 362 mμ (10,720).

Experimental

Yields of substances that have no definite m. p. refer to the stage when they appeared homogeneous in paper chromatography. Chromatograms were developed by the ascending technique, solvents being (A) butan-1-ol–5N-acetic acid (7 : 3), and (B) 3% aqueous ammonium chloride, and were viewed in ultraviolet light of wavelengths 254 and 365 mμ. Infrared spectra were determined for Nujol mulls.

Methyl 3-Hydroxyquinoxaline-2-carboxylate.—3-Hydroxyquinoxaline-2-carboxylic acid [19] (1·6 g.) suspended in dry methanol (100 c.c.) saturated with dry hydrogen chloride was refluxed for 2 hr. Refrigeration gave the *methyl ester* (1·48 g., 86%) which recrystallised from methanol as prisms, m. p. 222° (Found: C, 58·8; H, 3·5; N, 14·1. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 4·0; N, 13·7%).

Methyl 3 : 4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate (II; R = Me, R′ = H).—Methyl 3-hydroxyquinoxaline-2-carboxylate (12 g.), methyl iodide (20 g.), and anhydrous potassium carbonate (60 g.) were refluxed in dry acetone (180 c.c.) for 24 hr. The mixture was then cooled, water was added, and the whole extracted with chloroform. Evaporation of the dried chloroform extract, and recrystallisation of the residue from methanol gave the *N*-methyl ester (10 g., 78%) as rosettes of needles, m. p. 126 (lit.,[19] 126°).

Guanidine 3 : 4-Dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate.—(*a*) The above *N*-methyl ester (1·44 g.) and guanidine carbonate (0·6 g.) in 75% aqueous methanol (30 c.c.) were refluxed for 5 hr. On cooling, the *guanidine salt* (1·46 g., 84%) separated as yellow prisms, m. p. 248—249°. Recrystallisation from 75% aqueous methanol raised the m. p. to 252·5° (Found: C, 50·4; H, 4·6; N, 26·8. $C_{11}H_{13}O_3N_5$ requires C, 50·2; H, 5·0; N, 26·6%).

(*b*) The *N*-methyl ester (1 g.) and guanidine carbonate (3 g.) were ground and heated at 160—170° for 30 min., cooled, and dissolved in warm water (20 c.c.), and acetic acid was added to give pH 7. The solution was extracted with ether and chloroform (extracts rejected) and taken to dryness *in vacuo*. The yellow residue, recrystallised from aqueous methanol, gave the guanidine salt, m. p. and mixed m. p. 251°. The residual mother-liquors contained fluorescent substances which were not identified.

(*c*) An authentic sample of the guanidine salt was prepared by mixing the *N*-methyl acid (100 mg.) (prepared by hydrolysis of the methyl ester) and guanidine carbonate (45 mg.) in

[19] King and Clark-Lewis, *J.*, 1951, 3379.

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warm 75% aqueous methanol (3 c.c.); yellow prisms (82 mg.) separated almost immediately, having m. p. 251°.

2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-*Octahydro*-2-*imino*-4′-*methyl*-3′ : 5-*dioxoglyoxaline*-4-spiro-2′-*quinoxaline* (III; R = Me, R′ = H, R″ = NH).—Methyl 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate (3 g.) in dry methanol (70 c.c.) was added to a solution from sodium (0·75 g.) in dry methanol (70 c.c.). Dry powdered guanidine hydrochloride (1·35 g.) was added, and the mixture was refluxed for 30 min. The solution was concentrated *in vacuo* to *ca.* 30 c.c., cooled in ice-water, and diluted by addition of distilled water (40 c.c.). 2N-Hydrochloric acid was added dropwise to give pH 6·8, and the resulting precipitate was collected, washed with methanol (30 c.c.), and dried at 70° (yield, 2·92 g., 87%). Recrystallisation from water (200 c.c.) (charcoal) gave the spiro-*compound* as colourless needles, m. p. 229—230° (decomp.) (Found: C, 54·1; H, 4·2; N, 28·8. $C_{11}H_{11}O_2N_5$ requires C, 53·9; H, 4·5; N, 28·6%).

A solution of the *spiro*-compound (0·34 g.) in dry methanol (25 c.c.) saturated with dry hydrogen chloride was refluxed for 1 hr. The intense yellow precipitate which was formed gradually was collected and recrystallised from dry methanol, to give the *hydrochloride* (0·18 g., 46%) of the *spiro*-compound as yellow needles, m. p. 265—266° (Found: C, 47·1; H, 4·1; N, 24·8; Cl, 12·6. $C_{11}H_{11}O_2N_5$,HCl requires C, 46·9; H, 4·3; N, 24·9; Cl, 12·6%).

2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-*Octahydro*-4′-*methyl*-2 : 3′ : 5-*trioxoglyoxaline*-4-spiro-2′-*quinoxaline* (III; R = Me, R′ = H; R″ = O).—A similar condensation of the *N*-methyl ester (II; R = Me R′ = H) (1 g.) with sodium (0·24 g.) and urea (0·28 g.) in dry methanol (20 c.c.) gave an analogous *spiro*-compound (0·88 g., 78%). Recrystallisation from aqueous methanol gave colourless needles, m. p. 224—226° (decomp.) (Kuhling and Kazelitz [20] give m. p. 224° for the compound described as "methylaminophenyliminoalloxansaure;" Clark-Lewis [10] gives m. p. 238°) (Found: C, 53·4; H, 3·7. Calc. for $C_{11}H_{10}O_3N_4$: C, 53·7; H, 4·1%).

2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-*Octahydro*-1 : 3 : 4′-*trimethyl*-2 : 3′ : 5-*trioxoglyoxaline*-4-spiro-2′-*quinoxaline*.—The preceding spiran (0·425 g.), methyl iodide (2 c.c.), and anhydrous potassium carbonate (3 g.) were refluxed in dry acetone (25 c.c.) for 20 hr. The mixture was cooled, water was added, and the whole was extracted with chloroform (3 × 50 c.c.). The dried chloroform extracts were evaporated to dryness, and the residue recrystallised from ethanol, to give the trimethyl compound (0·32 g., 68%), m. p. 194° undepressed when mixed with an authentic sample prepared from 3-hydroxyquinoxaline-2-carboxyureide by Clark-Lewis's method.[10]

2-*Amino*-4-*hydroxybenzo*[g]*pteridine* (IV; R = H).—(*a*) A solution from sodium (0·347 g.) in dry propan-1-ol (40 c.c.) was added to a warm solution of dry guanidine hydrochloride (1·49 g.) in dry propan-1-ol (50 c.c.). The mixture was shaken, added to a hot solution of the *N*-methyl ester (II; R = Me, R′ = H) (1 g.) in dry propan-1-ol (50 c.c.), and refluxed for 90 hr. The resulting suspension was evaporated to dryness *in vacuo*, the residue was dissolved in water, and 2N-hydrochloric acid was added to give pH 6. The yellow gelatinous precipitate which separated was collected by centrifugation, washed with water, and dried. Recrystallisation from dimethylformamide (850 c.c.) gave 2-*amino*-4-*hydroxybenzo*[g]*pteridine* (0·55 g., 56%) as small prismatic needles, m. p. >360° (Found: C, 56·2; H, 3·3; N, 33·1. $C_{10}H_7ON_5$ requires C, 56·3; H, 3·3; N, 32·9%).

(*b*) Similar condensation of methyl 3-hydroxyquinoxaline-2-carboxylate (1 g.) with guanidine hydrochloride (1·49 g.) and sodium (0·345 g.) in propanol (150 c.c.) gave, after 17 hours' refluxing, the benzopteridine (0·56 g., 54%). The ultraviolet and infrared spectra of this material were identical with those of the specimen prepared as above.

(*c*) The *spiro*-compound (III; R = Me, R′ = H, R″ = NH) (0·4 g.), suspended in dry methanol (15 c.c.), was added to a solution from sodium (0·08 g.) in dry methanol (10 c.c.). The mixture was refluxed for 44 hr. and worked up as above, to give the benzopteridine (43 mg., 12%), identical with the material prepared as in (*a*) and (*b*).

Methylation of 2-*Amino*-4-*hydroxybenzo*[g]*pteridine* (IV; R = H).—The benzopteridine (126 mg.), methyl iodide (1 c.c.), and anhydrous potassium carbonate (2 g.) were refluxed in dry acetone (25 c.c.) for 24 hr. The mixture was shaken with water and chloroform (3 × 50 c.c.), and the chloroform extracts were dried and evaporated to dryness. Recrystallisation from methanol (charcoal) gave the *dimethyl derivative* (56 mg., 40%) of the benzopteridine as pale yellow needles, m. p. 350° (Found: C, 59·5; H, 4·5; N, 29·4. $C_{12}H_{11}ON_5$ requires C, 59·7; H, 4·6; N, 29·0%). Starting materials obtained by methods (*a*) and (*b*) gave identical products.

[20] Kuhling and Kazelitz, *Ber.*, 1906, **39**, 1314.

Ethylation of 2-Amino-4-hydroxybenzo[g]*pteridine* (IV; R = H).—Treatment of the benzopteridine prepared by methods (*a*) and (*b*) above with ethyl iodide in the presence of anhydrous potassium carbonate gave the *diethyl derivative* as pale yellow needles, m. p. and mixed m. p. 307—308° (decomp.) (Found: C, 62·4; H, 5·4; N, 25·7. $C_{14}H_{15}ON_5$ requires C, 62·4; H, 5·6; N, 26·0%), having identical ultraviolet and infrared spectra.

2 : 10-*Dihydro-4-hydroxy-2-imino-10-methylbenzo*[g]*pteridine* (I; R = Me, R′ = H).—Methyl 3 : 4-dihydro-4-methyl-3-oxoquinoxaline-2-carboxylate (1 g.) was condensed with guanidine (3 equivs.) as in the preparation of the alloxazine derivative (IV; R = H) above, except that the reaction was carried out in the dark and in oxygen-free nitrogen. The cooled reaction mixture yielded a bright orange precipitate (1·6 g.) readily separated by paper chromatography into the aminoalloxazine (IV; R = H) and the *iso*alloxazine 2-imine (I; R = Me, R′ = H). Chromatography of a larger sample (0·3 g.) on a column of cellulose powder (Whatman No. 1; 70 g.) with butan-1-ol–water–acetic acid (63 : 27 : 10) as solvent did not, however, separate the two components completely. The remainder of the crude product (1·3 g.) was dissolved in the minimum quantity of hot 5N-hydrochloric acid. The hydrochloride of the aminoalloxazine (IV; R = H) which separated on cooling was filtered off, and the filtrate was diluted with ethanol and evaporated to dryness *in vacuo*. The residue, when shaken with dry ethanol (100 c.c.), gave a bright orange powder (100 mg.). Recrystallisation from ethanol gave the bright yellow *isoalloxazine 2-imine* (I; R = Me, R′ = H), m. p. >350° (Found: C, 53·3; H, 4·0. $C_{11}H_9ON_5,H_2O$ requires C, 53·9; H, 4·5%).

Methyl 3 : 4-*Dihydro-6* : 7-*dimethyl-3-oxo-4-*D*-ribitylquinoxaline-2-carboxylate* (II; R = D-ribityl, R′ = Me).—To a solution of 3 : 4-dihydro-6 : 7-dimethyl-3-oxo-4-D-ribitylquinoxaline-2-carboxylic acid [11] (4·6 g.) in the minimum quantity of methanol was added ethereal diazomethane (8 equivs.). After 30 min., the solution was evaporated to dryness *in vacuo* and the residue recrystallised from methanol, to give the *methyl ester* (4·25 g., 89%) as pale yellow needles, m. p. 185—186° (Found: C, 55·9; H, 6·3; N, 7·6. $C_{17}H_{22}O_7N_2$ requires C, 55·7; H, 6·1; N, 7·7%).

2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-*Octahydro-2-imino-6′* : 7′-*dimethyl-3′* : 5-*dioxo-4′-*D*-ribitylglyoxaline*-4-spiro-2′-*quinoxaline* (III; R = D-*ribityl*, R′ = Me, R″ = NH).—To a solution from sodium (0·52 g.) in dry propan-1-ol (12·5 c.c.) was added dry powdered guanidine hydrochloride (0·225 g.) in propan-1-ol (12·5 c.c.). The mixture, after filtration, was added to a solution of the methyl ester (II; R = D-ribityl, R′ = Me) (0·25 g.) in dry propan-1-ol (12·5 c.c.) and kept at 25° for 20 hr. The cream-coloured precipitate was collected, washed with a little water, and dried, to give the spiro-*compound* (0·2 g., 75%), m. p. 183—186° (Found: C, 48·3; H, 6·6; N, 16·9. $C_{17}H_{23}O_6N_5,1{\cdot}5H_2O$ requires C, 48·6; H, 6·2; N, 16·7%).

A solution of the *spiro*-compound in 2N-hydrochloric acid gave the *hydrochloride*, yellow needles, m. p. 227—229° (from 2N-hydrochloric acid) (Found: C, 47·7; H, 5·9; N, 16·7. $C_{17}H_{23}O_6N_5,HCl$ requires C, 47·5; H, 5·6; N, 16·3%).

2-*Amino-4-hydroxy-7* : 8-*dimethylbenzo*[g]*pteridine* (IV; R = Me).—The methyl ester (II; R = D-ribityl, R′ = Me) (1 g.) was condensed with guanidine (from 0·85 g. of the hydrochloride and 0·2 g. of sodium) in propan-1-ol as in the preparation of the analogous aminoalloxazine (IV; R = H). Recrystallisation of the crude product (0·66 g.) from dimethylformamide gave the benzopteridine (" 2-aminolumichrome ") as yellow needles, m. p. >350° (Found: C, 59·7; H, 4·2; N, 28·6. Calc. for $C_{12}H_{11}ON_5$: C, 59·7; H, 4·6; N, 29·0%).

2 : 10-*Dihydro-4-hydroxy-2-imino-7* : 8-*dimethyl-10-*D*-ribitylbenzo*[g]*pteridine* (I; R = D-ribityl, R′ = Me).—The preceding condensation was repeated in the dark and in an atmosphere of oxygen-free nitrogen. The mixture was filtered while hot, and the crude orange-brown product (1·25 g.) was washed with ether and dried. This material, shown by paper chromatography to contain riboflavin 2-imine, was purified by one of the following methods:

(*a*) The crude material (1·25 g.) was dissolved in 50% acetic acid (300 c.c.), and the solution was neutralised with solid sodium hydrogen carbonate. The red insoluble material which separated was removed by centrifugation, and the supernatant solution was extracted with phenol (total 300 g.). Ether (1 l.) was added to the phenolic extracts which were re-extracted with water (90 c.c.). This aqueous solution deposited overnight a red product shown by paper chromatography to be largely riboflavin 2-imine. This was dissolved in the minimum of 5% acetic acid and chromatographed on Florisil (50 g.) in the dark. The column was washed with 5% acetic acid (100 c.c.), and the product finally eluted with 1 : 9 pyridine–water (150 c.c.). The eluate was taken to dryness *in vacuo* (rotatory evaporator), and the residue dissolved in

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the minimum of 2N-hydrochloric acid. Addition of solid sodium hydrogen carbonate to give pH 7 yielded the iso*alloxazine* 2-*imine* (" 2-iminoriboflavin ") as an orange powder (0·15 g., 15%) (Found: C, 54·1; H, 5·7; N, 18·2. $C_{17}H_{21}O_5N_5$ requires C, 54·4; H, 5·6; N, 18·7%).

(*b*) The crude product (1·2 g.) was dissolved in 2N-hydrochloric acid (100 c.c.). To the filtered solution were added a few drops of hydrogen peroxide to bleach any soluble impurities, and 10% aqueous sodium hydrogen carbonate was added to give pH 7. The resulting mixture was heated at 100° for 2 hr. to coagulate the precipitate, which was collected after being kept overnight at 0°. This procedure was repeated several times and finally gave riboflavin 2-imine (0·15 g.) as an orange powder. The infrared spectrum was identical with that of the specimen prepared as above.

Methyl 3 : 4-*Dihydro*-4 : 6 : 7-*trimethyl*-3-*oxoquinoxaline*-2-*carboxylate* (II; R = R′ = Me).—3 : 4-Dihydro-4 : 6 : 7-trimethyl-3-oxoquinoxaline-2-carboxylic acid [14] (2·8 g.) was esterified with diazomethane (8 equivs.). Recrystallisation from methanol gave the *methyl ester* (II; R = R′ = Me) (1·95 g., 66%) as yellow plates, m. p. 169—170° (Found: C, 63·8; H, 5·9; N, 11·4. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7; N, 11·4%).

2 : 3 : 4 : 5 : 1′ : 2′ : 3′ : 4′-*Octahydro*-2-*imino*-4′ : 6′ : 7′-*trimethyl*-3′ : 5-*dioxoglyoxaline*-4-spiro-2′-*quinoxaline* (III; R = R′ = Me, R″ = NH).—Methyl 3 : 4-dihydro-4 : 6 : 7-trimethyl-3-oxoquinoxaline-2-carboxylate (II; R = R′ = Me) (0·25 g.) was condensed with guanidine as in the preparation of the ribityl analogue (III; R = D-ribityl, R′ = Me, R″ = NH). Recrystallisation of the crude product from 2N-hydrochloric acid gave the *hydrochloride* of the *spiro*-compound as yellow needles, m. p. 267—270° (Found: C, 50·1; H, 5·4; N, 22·3. $C_{13}H_{15}O_2N_5$,HCl requires C, 50·4; H, 5·2; N, 22·6%).

The free *base* was prepared by dissolving the hydrochloride in water and adjusting the pH to 7 by the addition of solid sodium hydrogen carbonate. The pale cream precipitate was collected, washed with hot water, and dried *in vacuo* to give a hygroscopic powder, m. p. 275° (Found: C, 57·1; H, 5·5. $C_{13}H_{15}O_2N_5$ requires C, 57·1; H, 5·5%).

2 : 10-*Dihydro*-4-*hydroxy*-2-*imino*-7 : 8 : 10-*trimethylbenzo*[g]*pteridine* (I; R = R′ = Me).—To a solution of dimeric 3 : 4-dimethyl-*o*-benzoquinone [13] (0·32 g.) in water (10 c.c.) and 10% aqueous sodium hydroxide (1 c.c.) was added a similar solution of 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine [13] (V; R = Me) (0·4 g.). The mixture was kept at room temperature for 3 days in a stoppered flask. The resulting precipitate was collected, shaken with N-sodium hydroxide (25 c.c.) in which the *iso*alloxazine 2-imine is insoluble, and finally re-filtered and washed with ether. Recrystallisation from the minimum quantity of 2N-hydrochloric acid gave the *hydrochloride* (0·06 g.) of the benzopteridine as orange needles, m. p. >360° (Found: C, 53·1; H, 4·6; N, 24·2. $C_{12}H_{13}ON_5$,HCl requires C, 53·5; H, 4·8; N, 24·0%).

Treatment of the iso*Alloxazine* 2-*Imines* (I) *with Alkali*.—The imine (2 mg.) was heated in N-sodium hydroxide (1 c.c.) at 100° for 1 hr. in the dark. The products were examined by paper chromatography and ultraviolet spectroscopy. Riboflavin 2-imine (I; R = D-ribityl, R′ = Me) and lumiflavin 2-imine (I; R = R′ = Me) were converted completelyin to 2-aminolumichrome (IV; R = Me); and the 10-methyl*iso*alloxazine 2-imine (I; R = Me, R′ = H) was converted into 2-aminoalloxazine (IV; R = H). A similar change took place more slowly at room temperature.

Photolysis of Riboflavin 2-*Imine* (I; R = D-ribityl, R′ = Me).—Riboflavin 2-imine (5 mg.) in 0·1N-hydrochloric acid (5 c.c.) was irradiated for 16 hr. with ultraviolet light (Hanovia U.V.S. 500). Paper chromatography and ultraviolet spectroscopy then showed the presence of 2-aminolumichrome (IV; R = Me) and a little unchanged imine.

Similar photolysis in 0·5N-sodium hydroxide yielded lumiflavin 2-imine (I; R = R′ = Me), 2-aminolumichrome (IV; R = Me), and a product of unknown structure whose absorption spectrum (max. at 210, 270, and 370 mμ at pH 1), indicates that it is probably a quinoxaline.

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141. *Alkyls and Aryls of Transition Metals. Part I. Complex Methylplatinum*(II) *Derivatives.**

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A reason for the instability of the alkyl and aryl derivatives of transition metals is suggested. This leads to the conclusion that ligands causing large splittings of the *d*-energy levels should stabilise planar and octahedral complexes of d^2 to d^8 types. This has been explored for the d^8 planar complexes of the nickel Group, and this paper records the preparation and properties of a series of methylplatinum(II) derivatives stabilised by tertiary phosphines and a chelating organic disulphide as ligands. The types *trans*-$[(PR_3)_2PtMeX]$ and *cis*-$[(PR_3)_2PtMe_2]$ (X = halogen) are most stable and both are prepared by the action of methyl-lithium or methylmagnesium halide on *cis*- or *trans*-$[(PR_3)_2PtX_2]$. The less stable *cis*-$[(PEt_3)_2PtMeCl]$ was prepared by action of hydrogen chloride on the *cis*-dimethyl compound, but *trans*-$[(PR_3)_2PtMe_2]$ was not obtained pure. The isomerisation, cleavage, and addition reactions of the stable methylplatinous compounds are described. The addition of methyl iodide to *trans*-$[(PR_3)_2PtMeI]$ gives a platinum(IV) derivative $[(PR_3)_2PtMe_2I_2]$. Dipole moments are also recorded.

Transition metals do not form organometallic compounds in the same way as most other metals; instead their alkyl and aryl derivatives appear to be very unstable at room temperature.[1] Transition metals differ from the others in that the *d*-orbitals in their penultimate shells are on an energy level close to that of their valency *s*- and *p*-orbitals. In some way this must account for the instability of their organic derivatives. Perhaps it is because electrons can easily be promoted from the relatively high-energy filled *d*-orbitals into antibonding σ-orbitals of the metal-to-carbon bond, or, if the *d*-orbitals are empty, from the carbon-to-metal bonding orbitals into a *d*-orbital, in either case weakening the metal-to-carbon bond. At any rate it appears (*a*) that for the formation of stable organometallic compounds it is essential to have more than a certain minimum difference in energy (ΔE) (Fig. 1) between the highest-energy orbital which contains electrons and the lowest-energy orbital which is vacant, and (*b*) that in most transition-metal compounds with their rather close *d*-energy levels this minimum is not attained.

Starting from this premise we have been able to isolate a number of very stable complex alkyl and aryl derivatives of Group VIII metals by adjusting the energy levels of the *d*-orbitals by co-ordination. These have the general formula $L_lMX_mR_n$, where L is an uncharged ligand, M the transition metal, X a halogen atom, and R an alkyl or aryl group. To the present we have concerned ourselves only with complexes where the *d*-orbitals not used in σ-bonding are at least singly occupied, *i.e.*, metals in the second half of the transition series Fe(II), Co(II), Ni(II), Cu(I), and their analogues. The energy levels of these non-σ-bonding *d*-orbitals in the penultimate shells of the metal atoms lie below those of the antibonding σ-levels. They constitute the highest occupied energy level in the complex. The lowest vacant level is an antibonding σ-orbital (or, according to crystal-field theory, a vacant *d*-orbital directed towards the ligands). It appeared to us that the best way to increase the energy difference between these levels would be to lower still further the energy of the non-σ-bonding *d*-orbitals by combining them with π-type orbitals of low energy in suitable ligands. In terms of molecular-orbital theory, to form stable organo–transition-metal complexes, with all the *d*-orbitals either occupied or used in bond formation, we need to combine the metal with ligands, L, capable of forming strong dative π-bonds with the metal. In terms of ligand-field theory, in those complexes where one or more

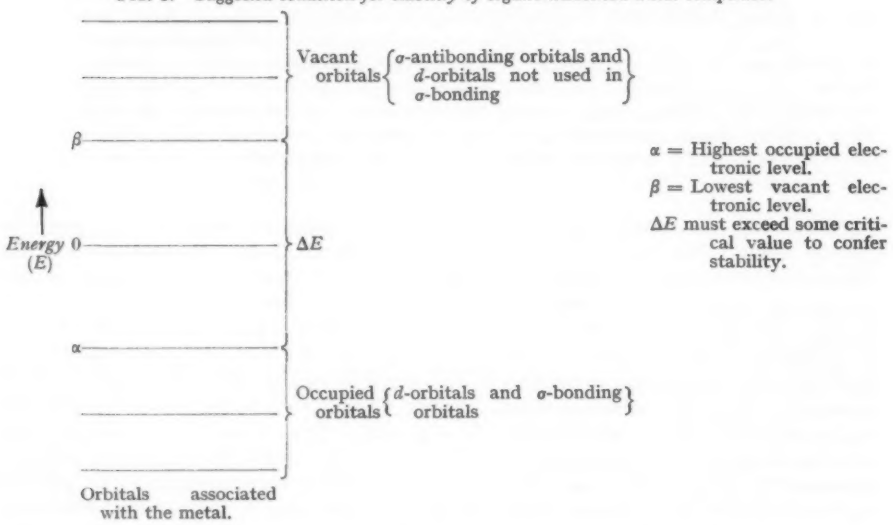
* A brief account of this work formed part of a paper read before the American Chemical Society at its April, 1958, Meeting in San Francisco.

[1] Cotton, *Chem. Rev.*, 1955, **55**, 551.

d-orbitals are used in hybridisation to form σ-bonds we need ligands with a strong field causing sufficiently large ligand field splittings in the energy levels of the *d*-shell.*

If these views are correct the stability of organo-transition-metal complexes with their *d*-orbitals either occupied or used in σ-bond formation will be greater when the ligands are in square planar and octahedral than when they are in tetrahedral configurations. This follows because ligands in orthogonal relationship form stronger dative π-bonds than when they are in tetrahedral positions. Also, since double-bonding and ligand field splittings are greater in the heavier transition-metal complexes than in the corresponding light transition-metal complexes, the heavier transition metals should form the more stable organometallic compounds, having *occupied* non-σ-bonding *d*-orbitals (Fig. 1).[3]

FIG. 1. *Suggested condition for stability of organo-transition-metal complexes.*



This is the reverse of what is found in the rest of the Periodic Table, where the heaviest element in each Sub-group forms the least stable alkyl and aryl derivatives. The only exception is the zinc Group where there is a mixed sequence of thermal stabilities $ZnR_2 > CdR_2 < HgR_2$,[4] and a completely reversed sequence of chemical reactivities. Presumably there is sufficient transition-metal character in this Group to cause the irregularity in these sequences.

To test these views we have examined the organometallic derivatives of the nickel Group of elements in their bivalent state, using tertiary organic phosphines to adjust the energy levels of the *d*-orbitals. Phosphines were chosen because they appear to be the most strongly double-bonding to the metal of all ligands except those containing carbon as ligand atoms, *e.g.*, CO and C_2H_4;[5] also they form very stable complexes of the type

* At the beginning of the transition-metal series (*e.g.*, Ti, V) where the non-σ-bonding *d*-orbitals are empty, we need to increase the energy difference between them and the σ-bonding orbitals. This requires electronegative ligands with small ligand field strengths. Therefore a compromise must be struck between electronegativity and ligand field strengths as in the organotitanium compounds, *e.g.*, $TiPh(OPr^i)_3$.[2]

[2] Herman and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 3877, 3882.

[3] Griffith and Orgel, *Quart. Rev.*, 1957, **11**, 381; Jörgensen, Tenth Solvay Conference in Chemistry, R. Stoops, Brussels, 1956, p. 355; Chatt, Gamlen, and Orgel, *J.*, 1958, 486.

[4] Rochow, Hurd, and Lewis, "The Chemistry of Organo-metallic Compounds," Wiley, New York, 1957, p. 105.

[5] Chatt, Duncanson, and Venanzi, *J.*, 1958, 3203, and previous references therein.

$[(PR_3)_2MX_2]$ (M = Ni, Pd, and Pt; X = halogen) of square planar configuration and suitable for this study.

On treating the above complexes in ether at room temperature with alkyl- and aryl-lithium or similar Grignard reagents we isolated stable organometallic derivatives of the three metals. Their stabilities fall rapidly in the order Pt > Pd > Ni in analogous compounds, in accordance with the views expressed above. Only the platinum(II) and nickel(II) compounds have been examined in detail because we learnt during the progress of this work that Professor G. E. Coates [6] had independently prepared similar compounds and was making a detailed study of those of palladium(II).

Whilst this work was in progress a number of alkyl and aryl derivatives of transition metals, stabilised by co-ordination to the *cyclo*pentadienyl anion or carbon monoxide, or both, have been reported, *e.g.*, $[Ti(C_5H_5)_2Ph_2]$,[7] $[(CO)_5MnMe]$,[8] $[C_5H_5Mo(CO)_3Me]$,[9] and with nitric oxide, $[C_5H_5Cr(NO)_2Me]$.[9] There is also the very unstable compound $[Co(CO)_4Me]$.[10] Similarly the olefinic double bond has been shown to stabilise a metal–alkyl bond in some complex chelate derivatives of platinum(II) and palladium(II).[11] These all have filled *d*-orbitals and fit into the above scheme. The recently discovered chromium(III) organic derivatives $[Cr(H_2O)_5{\cdot}CH_2Ph]$ [12] and $[Cr(Thf)_3Ph_3]$ [13] (Thf = tetrahydrofuran) are not exactly in this category because the ligands are not strongly double-bonding. However, with their singly occupied non-σ-bonding *d*-orbitals the tendency for electrons to be promoted into anti-bonding σ-orbitals must be very small, and so they accord with our original premise.

It should be noted that those electronic configurations which occur in stable organo-transition-metal complexes are just those which Taube [14] has pointed out as occurring in non-labile complexes with the common ligands.

In this paper we shall describe in detail only methylplatinum(II) compounds. Their study was started in 1952 in collaboration with Dr. M. E. Foss at Gloucester Technical College. He prepared the first well-defined methyl derivative, *trans*-$[(PPr^n_3)_2PtMeI]$, and studied its reaction to give $[(PPr^n_3)_2PtMe_2I_2]$, but then had to abandon the work. Methylplatinum(II) compounds were previously unknown, unless some of the ill-defined substances described by Gilman and Lichtenwalter [15] are eventually found to be of this type. Here we describe new compounds of the types *trans*-$[(PR_3)_2PtMeX]$ and *cis*-$[(PR_3)_2PtMe_2]$ (where R = Et, Pr^n, and Ph, and X = Cl, Br, I, SCN, and NO_3), and the less stable *cis*-$[(PEt_3)_2PtMeCl]$. Pure *trans*-$[(PEt_3)_2PtMe_2]$ is difficult to obtain. The stable chelate compounds $[(Et_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PEt_2)PtMe_2]$ and $[(EtS{\cdot}CH_2{\cdot}CH_2{\cdot}SEt)PtMe_2]$ are also described.

Methylplatinum(II) compounds, stabilised by combination with tertiary phosphines, are remarkably inert, colourless, and crystalline. They are not hydrolysed by dilute acids or oxidised in moist air, and appear stable indefinitely (no deposition of metallic platinum). A sample of *trans*-$[(PEt_3)_2PtMeI]$ is unchanged after a year and one of *trans*-$[(PPr^n_3)_2PtMeI]$ has not deposited platinum during six years. They are soluble in organic solvents and insoluble in water. *cis*$[(PEt_3)_2PtMe_2]$ distils without decomposition at $85°/10^{-4}$ mm., but not at higher temperatures (100—130°) and pressures (0·05—12 mm.). The derivatives *trans*-$[(PEt_3)_2PtMeX]$ (where X = Cl, Br, I) and *cis*-$[(PEt_3)_2PtMeCl]$ can be purified by chromatography on alumina (Spence Grade "H") with some loss, but *cis*-$[(PEt_3)_2PtMe_2]$ is recoverable from the column only in poor yield.

[6] Calvin and Coates, *Chem. and Ind.*, 1958, 160.
[7] Summers and Uloth, *J. Amer. Chem. Soc.*, 1954, **76**, 2278.
[8] Coffield, Kozikowski, and Closson, *J. Org. Chem.*, 1957, **22**, 598.
[9] Piper and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **3**, 104.
[10] Hieber, Vohler, and Braun, *Z. Naturforsch.*, 1958, **13b**, 192.
[11] Chatt, Vallarino, and Venanzi, *J.*, 1957, 2496, 3413.
[12] Anet and Leblanc, *J. Amer. Chem. Soc.*, 1957, **79**, 2649.
[13] Herwig and Zeiss, *ibid.*, p. 6561.
[14] Taube, *Chem. Rev.*, 1952, **50**, 69.
[15] Gilman and Lichtenwalter, *J. Amer. Chem. Soc.*, 1938, **60**, 3085; 1939, **61**, 957; Lichtenwalter, *Iowa State Coll. J. Sci.*, 1939, 1457; cf. Gilman, Lichtenwalter, and Benkeser, *J. Amer. Chem. Soc.*, 1953, **75**, 2063.

Preparations.—In general, a mixture of the mono- and di-methyl derivative is obtained by the reaction of either *cis*- or *trans*-$[(PR_3)_2PtX_2]$ with methylmagnesium halide. These are not easily separable and, since the use of the theoretical quantity of Grignard reagent leaves some of the starting material in the mixture, a large excess of Grignard reagent was usually used. The ratio of products *trans*-$[(PR_3)_2PtMeX]$, *cis*-$[(PR_3)_2PtMe_2]$, and *cis*-$[(PR_3)_2PtMeX]$ depends upon the halogen X and the configuration of the starting material. Attempts to isolate *trans*-$[(PR_3)_2PtMe_2]$ failed.

The highest proportion of the *trans*-monomethyl compound is produced by the use of *trans*-starting material and the Grignard iodide. Thus *trans*-$[(PEt_3)_2PtMeI]$ is obtained in 90% yield by use of a large excess of iodide at 20°. Even use of a higher reaction temperature (80°) still gives *trans*-$[(PEt_3)_2MeI]$ in good yield and no isolatable quantity of the dimethyl derivative, suggesting that the proportions of the two products depend in this case on thermodynamic rather than kinetic factors. The use of *cis*-starting material or of the lighter halogens increases the proportion of dimethyl derivative, but even the reaction of *cis*-$[(PR_3)_2PtCl_2]$ with a large excess of methylmagnesium chloride will not give the latter pure. It is best prepared by the use of methyl-lithium (prepared from methyl chloride). *cis*-$[(PEt_3)_2PtMe_2]$ is obtained in 88% yield by reaction of the *cis*-dichloride with a 10% excess of methyl-lithium, and the analogues $C_2H_4(PEt_2)_2PtMe_2$ and $C_2H_4(SEt)_2PtMe_2$ are prepared similarly.

The monomethyl derivatives, when present in large proportion, are best removed from *cis*-$(PEt_3)_2PtMe_2$ by treating the mixture in ethanol with thiourea. This forms easily separable complexes with the mono-, leaving the di-methyl derivative.

The compound *cis*-$[(PEt_3)_2PtMeCl]$ is probably an intermediate in the formation of *cis*-$[(PEt_3)_2PtMe_2]$ from *cis*-$[(PEt_3)_2PtCl_2]$ by the Grignard or methyl-lithium procedure, but was isolated only in very small quantity; it was obtained also in similar quantity from some preparations of *trans*-$[(PEt_3)_2PtMeCl]$ from *trans*-$[(PEt_3)_2PtCl_2]$.

Many possible methods of preparation were tried but only the cleavage of *cis*-$[(PEt_3)_2PtMe_2]$ by dry hydrogen chloride was satisfactory. Stoicheiometric quantities of the reagents in ether gave a quantitative yield at room temperature.

cis-$[(PEt_3)_2PtMeCl]$ is stable in benzene solution, but a trace of triethylphosphine causes rapid and almost complete isomerisation. In contrast, *trans*-$[(PEt_3)_2PtMeCl]$ was almost unchanged after 2 weeks in the presence of free triethylphosphine, and no *cis*-$[(PEt_3)_2PtMeCl]$ was isolated from the solution.[16]

trans-$[(PEt_3)_2PtX_2]$ (X = Cl or Br) reacts with the corresponding methylmagnesium halide at 20° much more slowly than does the *cis*-isomer, to give the monomethyl compound as the major product. At 80° the second halogen atom is partially replaced, but only the *cis*-dimethyl derivative can be isolated. Similarly from the reaction of methyl-lithium (2·2 mol. at 20°) the only dimethyl derivative isolated has a *cis*-configuration.

Repeated distillation of *cis*-$[(PEt_3)_2PtMe_2]$ (m. p. 81—82°) at 130°/12 mm. gave a product of low m. p. (almost completely molten at 57°) but identical analysis. This product also had a low dipole moment and was probably a mixture of *cis*- and *trans*-$[(PEt_3)_2PtMe_2]$. A very small quantity of the substantially pure *trans*-isomer (m. p. 76—79°) was isolated by chromatography.

Methylplatinum(II) derivatives stabilised by tri-*n*-propylphosphine and by triphenylphosphine were also prepared. The monomethyl compound, *trans*-$[(PPh_3)_2PtMeI]$, is difficult to separate from the dimethyl analogue and so is more readily obtained by reaction of methyl iodide with tris(triphenylphosphine)platinum(0):[17]

$$[Pt(PPh_3)_3] + 2MeI \longrightarrow \textit{trans}\text{-}[(PPh_3)_2PtMeI] + [PPh_3Me]I$$

This is an interesting reaction since it produces the methylplatinum compound without intervention of any other organometallic substance.

[16] Cf. Chatt and Wilkins, *J.*, 1951, 2532.
[17] Malatesta and Cariello, Internat. Conf. on Co-ordination Compounds, Rome, 1957; *J.*, 1958, 2323.

The methyl derivatives prepared during this work are listed in Table 1. The dipole moments were used to determine their configurations. The reactions of *trans*-[$(PEt_3)_2PtMeCl$], *trans*-[$(PEt_3)_2PtMeI$], and *cis*-[$(PEt_3)_2PtMe_2$] were studied as typical of the commoner derivatives.

TABLE 1.

Substance	M. p.	Dipole moment (±0·1; D)	Substance	M. p.	Dipole moment (±0·1; D)
A. Methylplatinum(II) *complexes.*					
cis-[$(PEt_3)_2PtMe_2$]	81—82°	5·65	*trans*-[$(PPr^n_3)_2PtMeI$]	47—48°	(3·9)
trans-[$(PEt_3)_2PtMeI$]	71—71·5	4·1	*cis*-[$(PPh_3)_2PtMe_2$]	235—237 †	5·45
trans-[$(PEt_3)_2PtMeBr$]	87—90	(3·7) *	[$(PPh_3)_2PtMeI$]	270—274	‡
trans-[$(PEt_3)_2PtMeCl$]	99—100	3·4	*trans*-[$(PPh_3)_2Pt(Me)SCN$]	247—249	(6·5)
cis-[$(PEt_3)_2PtMeCl$]	113—116 †	(8·4)	[$(Et_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PEt_2)PtMe_2$]	74·5—75·5	(6·7)
trans-[$(PEt_3)_2Pt(Me)SCN$]	93—95	6·65	[$(EtS{\cdot}CH_2{\cdot}CH_2{\cdot}SEt)PtMe_2$]	50—51	—
trans-[$(PEt_3)_2Pt(Me)NO_3$]	56—58	(6·0)			
B. New methylplatinum(IV) *complexes.*					
[$(PEt_3)_2PtMe_2I_2$]	101—103° †	5·85	[$(PPr^n_3)_2PtMe_2I_2$]	128° †	(5·8)
[$(PEt_3)_2PtMe_2Cl_2$]	114—117	(5·3)			

* Values in parentheses were calculated by using estimated refractivities and densities. Since the moments are high this introduces only an insignificant error. The margin of error (0·1 D) is determined by the uncertainty in the atom polarisation which may be up to 20% of the electron polarisation in complex compounds. † Decomp. ‡ Insol. in benzene.

Replacement of Halogens.—The halogen atoms of the monomethyl derivatives are readily replaced by treatment with an appropriate salt. Thus [$(PEt_3)_2PtMeCl$] is converted almost quantitatively into the corresponding bromide and iodide by treatment with the corresponding alkali-metal salts in acetone, *e.g.*:

$$trans\text{-}[(PEt_3)_2PtMeCl] + LiBr \longrightarrow trans\text{-}[(PEt_3)_2PtMeBr] + LiCl$$

Similarly, *trans*-[$(PEt_3)_2PtMeI$] is converted into the thiocyanate by treatment with potassium thiocyanate and, in smaller yield, into the nitrate by treatment with silver nitrate in aqueous methanol.

Cleavage of the Methyl Group from the Metal.—This was investigated in attempts to find a route to *cis*-[$(PR_3)_2PtMeX$]. The methyl groups are rapidly removed from the metal at room temperature by reaction with iodine, magnesium iodide, or hydrogen chloride in ether, and one methyl group from the dimethyl complex by *cis*-[$(PEt_3)_2PtCl_2$] in boiling benzene. Methyl iodide also causes cleavage (see addition reactions), *e.g.*:

$$cis\text{-}[(PEt_3)_2PtMe_2] \xrightarrow{I_2} trans\text{-}[(PEt_3)_2PtMeI] + MeI$$

$$trans\text{-}[(PEt_3)_2PtMeI] \xrightarrow{I_2} trans\text{-}[(PEt_3)_2PtI_2] + MeI$$

$$cis\text{-}[(PEt_3)_2PtMe_2] \xrightarrow{MgI_2} trans\text{-}[(PEt_3)_2PtI_2] + trans\text{-}[(PEt_3)_2PtMeI] + MeMgI$$

$$cis\text{-}[(PPh_3)_2PtMe_2] \xrightarrow{MgI_2} trans\text{-}[(PPh_3)_2PtMeI] + MeMgI$$

$$cis\text{-}[(PEt_3)_2PtMe_2] \xrightarrow{HCl} cis\text{-}[(PEt_3)_2PtMeCl] + CH_4$$

$$cis\text{-}[(PEt_3)_2PtMe_2] \xrightarrow{2HCl} cis\text{-}[(PEt_3)_2PtCl_2] + 2CH_4$$

In the first two of these reactions there is no evidence for the formation of a platinic compound [$(PEt_3)_2PtMe_nI_{4-n}$] stable at room temperature, but in the third reaction (with magnesium iodide in ether) there is an immediate precipitate when the components are mixed, which is evidence for the formation of an intermediate complex since both the reactants and the final products are soluble in ether.

Reaction of *cis*-[$(PEt_3)_2PtCl_2$] with *cis*-[$(PEt_3)_2PtMe_2$] (1·1 mol.) in hot benzene rapidly gives a mixture containing *cis*- and *trans*-[$(PEt_3)_2PtCl_2$], *cis*-[$(PEt_3)_2PtMe_2$], and *trans*-[$(PEt_3)_2PtMeCl$]. This variety of products suggests that some free triethylphosphine is

formed and causes isomerisation of the *cis*-$[(PEt_3)_2PtCl_2]$.[16] Reaction in the presence of a small quantity of the bridged complex $[(PEt_3)_2Pt_2Cl_4]$, which reacts immediately with any free phosphine, is much slower, no *trans*-$[(PEt_3)_2PtCl_2]$ is found and in addition to unchanged starting material and *trans*-$[(PEt_3)_2PtMeCl]$ a small quantity of *cis*-$[(PEt_3)_2PtMeCl]$ is isolable.

Addition Reactions.—(a) *Methyl iodide.* The monomethyl derivatives add methyl iodide at 100°, producing platinic compounds, *e.g.*, $[(PEt_3)_2PtMe_2I_2]$, m. p. 101—103° and $[(PPr^n_3)_2PtMe_2I_2]$, m. p. 128°. This is analogous to the reaction which, it has been suggested, is responsible for the production of $(Me_3PtI)_4$ from platinous salts by reaction with methylmagnesium iodide in presence of an excess of methyl iodide.[18] The methyl iodide in $[(PEt_3)_2PtMe_2I_2]$ is rather loosely held and is removed in 3 hours at 80°/0·01 mm., or slowly in boiling solvents. It is not held as solvent of crystallisation because this product cannot be obtained from a solution of the monomethyl derivative in methyl iodide at room temperature, or even, except in very poor yield, at the boiling point of methyl iodide. When the components are heated in a sealed tube at 100° for a prolonged time (20 hours) cleavage of the methyl groups occurs:

$$[(PEt_3)_2PtMe_2I_2] \longrightarrow [(PEt_3)_2PtI_2] + C_2H_6$$

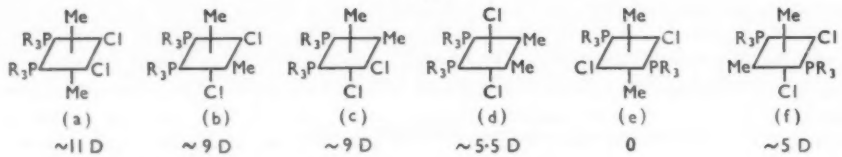
Iodine does not react with $[(PEt_3)_2PtMe_2I_2]$ in cold benzene, but on 15 minutes' boiling the methyl groups are eliminated. This reaction may occur through dissociation of the platinum(IV) complex, $[(PEt_3)_2PtMe_2I_2] \longrightarrow$ *trans*-$[(PEt_3)_2PtMeI] + MeI$, followed by fission with iodine as above.

Methyl iodide did not react with *trans*-$[(PEt_3)_2PtI_2]$, whence we expected to obtain $[(PEt_3)_2PtMeI_3]$, and with *cis*-$[(PEt_3)_2PtMe_2]$ it gave a mixture which was not separated.

(b) *Chlorine.* *cis*-$[(PEt_3)_2PtMe_2]$ reacts with two equivalents of chlorine to give $[(PEt_3)_2PtMe_2Cl_2]$.

(c) *Iodine.* In contrast, iodine causes cleavage of *cis*-$[(PEt_3)_2PtMe_2]$ (see above). This failure to give a stable platinic derivative must mean that the addition gives an isomeric form of $[(PEt_3)_2PtMe_2I_2]$ which is unstable and rapidly decomposes at room temperature.

FIG. 2.



The Configuration of the Dimethylplatinum(IV) *Complexes.*—Six stereoisomers of $[(PEt_3)_2PtMe_2Cl_2]$ are possible and estimates of their dipole moments are given in Fig. 2; two of these isomers (b and c) are mirror images. The dipole moments were estimated by assuming that the bond moments in the octahedral platinum(IV) complexes are approximately the same as in planar platinum(II) complexes. Thus, (a) would have a moment almost identical with that of *cis*-$[(PEt_3)_2PtCl_2]$ (10·9 D),[19] and (d) with *cis*-$[(PEt_3)_2PtMe_2]$ (5·55 D). The dipole moments of (b) and (c) would be the vector sum of the moments of *cis*-$[(PEt_3)_2PtMeCl]$ (8·4 D) and the system Me–Pt–Cl acting at right angles. The latter is the moment of *trans*-$[(PEt_3)_2PtMeCl]$ (3·4 D), and so the estimated moment of (b) and (c) is approximately $[(8\cdot4)^2 + (3\cdot4)^2]^{\frac{1}{2}} = 9\cdot1$ D. Form (f) would similarly have a moment compounded from the vector sum of two Me–Pt–Cl systems at right angles, *i.e.*, $[(3\cdot4)^2 + (3\cdot4)^2]^{\frac{1}{2}} = 4\cdot8$ D.

We expect that the dipole moments of the iodides $[(PEt_3)_2PtMe_2I_2]$ corresponding to

[18] Chatt and Duncanson, *J.*, 1953, 2939.
[19] Chatt and Wilkins, *J.*, 1952, 4300.

(d) and (e) would be similar to those of the chlorides; the others, where the iodine atoms are in *cis*-relation, might have dipole moments up to 1 D greater {compare *trans*-[$(PEt_3)_2PtMeCl$] and the corresponding iodide in Table 1*B*}.

The complex methylplatinic chloride and iodide listed in Table 1*B* have dipole moments of 5·3 and 5·8 D, respectively, and so must have configurations as (d) or (f).

Experimental

Microanalyses are by Messrs. W. Brown and A. G. Olney of these laboratories.

The complex platinous halides were prepared by established methods,[16,20] and 1 : 2-bis-(diethylphosphino)ethane as described by Wymore.[21] M. p.s were determined on a Kofler hot-stage and are corrected. Spence alumina (grade " H ") was used for chromatography.

trans-*Bis(triethylphosphine)iodo(methyl)platinum* [$(PEt_3)_2PtMeI$].—A solution of methylmagnesium iodide was prepared from methyl iodide (10·0 g.), magnesium (1·52 g.), and ether (60 c.c.). Benzene (20 c.c.) was added, followed by a solution of *trans*-bis(triethylphosphine)-dichloroplatinum (8·00 g.) in benzene (50 c.c.). After 1 hour's stirring at 20° dilute hydrochloric acid was added slowly with ice-cooling. The organic layer was separated, washed with water, and dried ($MgSO_4$). Evaporation of the solvent and crystallisation of the residue from methyl alcohol containing a little water afforded trans-*bis(triethylphosphine)iodo(methyl)platinum* (8·28 g., 90%) as colourless plates (Found: C, 27·2; H, 5·8%; *M*, ebullioscopically in 1·44% benzene solution, 568; *M*, in 2·28% benzene solution, 537. $C_{13}H_{33}IP_2Pt$ requires C, 27·2; H, 5·8%; *M*, 573). The compound was non-conducting in nitrobenzene solution. It was also prepared, in 40% yield, from *cis*-bis(triethylphosphine)dichloroplatinum and methylmagnesium iodide under similar conditions.

trans-*Bis(tri*-n-*propylphosphine)iodo(methyl)platinum* [$(PPr^n_3)_2PtMeI$].—This *compound* was similarly prepared from *cis*- or *trans*-bis(tri-*n*-propylphosphine)dichloroplatinum and formed plates (Found: C, 34·9; H, 6·5%; *M*, ebullioscopically in 1·8% benzene solution, 630; *M*, in 2·58% benzene solution, 626. $C_{19}H_{45}IP_2Pt$ requires C, 34·7; H, 6·9%; *M*, 657).

trans-*Bis(triethylphosphine)bromo(methyl)platinum* [$(PEt_3)_2PtMeBr$] was similarly prepared from methylmagnesium bromide (magnesium, 0·65 g.; ether, 25 c.c.) and *cis*-bis(triethylphosphine)dibromoplatinum (2·00 g.). Crystallisation, once from light petroleum (b. p. 60—80°), and several times from methyl alcohol, gave the pure complex as elongated prisms (Found: C, 29·7; H, 6·3. $C_{13}H_{33}BrP_2Pt$ requires C, 29·7; H, 6·3%).

trans-*Bis(triethylphosphine)chloro(methyl)platinum* [$(PEt_3)_2PtMeCl$].—Methylmagnesium chloride was prepared from magnesium (0·96 g.), ether (80 c.c.; plus iodine) and dry methyl chloride. *trans*-Bis(triethylphosphine)dichloroplatinum (2·0 g.) was added, and, after 1 hour's stirring at 20° the colourless mixture was hydrolysed with ice and hydrochloric acid. The residue from evaporation of the dried (magnesium sulphate) ether layer was chromatographed in light petroleum (b. p. 40—60°; 15 c.c.) containing ether (3 c.c.) on alumina (100 g.). Elution with light petroleum (b. p. 40—60°) containing ether (20% v/v) afforded trans-*bis(triethylphosphine)chloro(methyl)platinum* (1·1 g., 61%) as needles from light petroleum (b. p. 60—80°) (Found: C, 32·4; H, 6·9. $C_{13}H_{33}ClP_2Pt$ requires C, 32·4; H, 6·9%). Elution with ether gave needles (0·12 g.), m. p. 109—114° (decomp.), which, after two crystallisations from light petroleum (b. p. 60—80°), afforded long, very thin needles of cis-*bis(triethylphosphine)chloro(methyl)platinum* (Found: C, 32·7; H, 6·9%).

cis-*Bis(triethylphosphine)dimethylplatinum* [$(PEt_3)_2PtMe_2$] (*Grignard Method*).—Methylmagnesium chloride was prepared from magnesium (0·96 g.), ether (75 c.c.), iodine, and gaseous methyl chloride. *cis*-Bis(triethylphosphine)dichloroplatinum (3·00 g.) was added, and the mixture stirred for 1 hr. and hydrolysed by pouring it on ice and dilute hydrochloric acid. The ether layer was dried ($MgSO_4$) and evaporated under reduced pressure. Two crystallisations from light petroleum (cooling to −10°) and one from methyl alcohol gave colourless prisms (1·05 g.). These were warmed to 80° with a solution of thiourea (2 g.) in aqueous methanol (7 c.c. of H_2O, 3 c.c. of MeOH), and, after cooling, the solid was filtered off and dissolved in ether. After drying ($MgSO_4$), the ether was removed under reduced pressure and the residue recrystallised from light petroleum (b. p. 60—80°), to give cis-*bis(triethylphosphine)dimethylplatinum* (0·55 g.)

[20] Jensen, *Z. anorg. Chem.*, 1936, **229**, 237; Chatt and Venanzi, *J.*, 1955, 2787.
[21] Wymore, Ph.D. Thesis, 1957, Univ. Illinois; *Diss. Abs.*, 1957, **17**, 1208.

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as colourless prisms (Found: C, 36·7; H, 7·9%; *M*, ebullioscopically in 1·52% benzene solution, 485; *M*, in 2·25% benzene solution, 473. $C_{14}H_{36}P_2Pt$ requires C, 36·45; H, 7·85%; *M*, 461).

cis-*Bis(triphenylphosphine)dimethylplatinum* $[(PPh_3)_2PtMe_2]$.—Methylmagnesium bromide was prepared from gaseous methyl bromide, ether (50 c.c.), and magnesium (1·2 g.). Benzene (50 c.c.) was added, followed by *cis*-bis(triphenylphosphine)dichloroplatinum (3·00 g.), and the mixture was heated under reflux for 2 hr. After cooling to −10° the mixture was cautiously hydrolysed with dilute hydrobromic acid, and the white precipitate was filtered off. A further quantity was obtained from the organic layer on evaporation. The combined product was heated under reflux for 1 hr. with thiourea (1·0 g.) in ethyl alcohol (50 c.c.) and benzene (10 c.c.), and the whole was filtered hot. The residue, on crystallisation from benzene, afforded cis-*bis(triphenylphosphine)dimethylplatinum* as colourless prisms (1·64 g.) (Found: C, 60·9; H, 4·9. $C_{38}H_{36}P_2Pt$ requires C, 60·9; H, 4·85%).

1 : 2-*Bis(diethylphosphino)ethanedichloroplatinum* $[C_2H_4(PEt_2)_2PtCl_2]$.—*trans*-Bis(dimethyl sulphide)dichloroplatinum (3·42 g.) in chloroform (30 c.c.) was treated with 1 : 2-bis(diethylphosphino)ethane (1·88 g.) in an atmosphere of nitrogen. After 2 minutes' boiling the solution was cooled and light petroleum (b. p. 80—100°) was added. The precipitate was collected and dissolved in hot dilute ammonia, the mixture filtered, and the solution acidified at 0° with concentrated hydrochloric acid. The resultant precipitate was washed with water and crystallised from methyl alcohol, to give 1 : 2-*bis(diethylphosphino)ethanedichloroplatinum* (1·06 g.) as colourless prisms, m. p. 291—295° (with sublimation) (Found: C, 25·25; H, 5·15. $C_{10}H_{24}Cl_2P_2Pt$ requires C, 25·45; H, 5·15%).

Preparation of Methyl-lithium Solution.—This was prepared, in a typical case, from lithium (3 g.), ether (150 c.c.), and methyl chloride (about 50% of the theoretical quantity). To ensure that no unchanged methyl chloride remained the solution was stirred for at least 1 hr. after the addition. It was then filtered through asbestos and estimated by titration against 0·1N-hydrochloric acid.

Preparation of Dimethylplatinum(II) *Derivatives by Methyl-lithium. General Method.*—The finely divided platinous chloride complex (*cis*-isomer), suspended in dry benzene, was treated with ethereal methyl-lithium (10% excess) at 20°. After 15 min., light petroleum (10 c.c.; b. p. 60—80°) was added, the precipitated lithium chloride filtered off, and the product isolated by evaporating the solvent at 15 mm. and recrystallising the residue from light petroleum (b. p. 40—60°). Alternatively the lithium salts were removed by water, and the product was isolated from the organic layer. Prepared by the general method were: *cis*-bis(triethylphosphine)dimethylplatinum (yield 88%); 1 : 2-*bis(diethylphosphino)ethanedimethylplatinum*, colourless prisms (80%) (Found: C, 33·65; H, 7·1. $C_{12}H_{30}P_2Pt$ requires C, 33·4; H, 7·0%); and 1 : 2-*di(ethylthio)ethanedimethylplatinum*, colourless needles (66%) (Found: C, 25·6; H, 5·3. $C_8H_{20}S_2Pt$ requires C, 25·6; H, 5·35%).

cis-*Bis(triethylphosphine)chloro(methyl)platinum* $[(PEt_3)_2PtMeCl]$.—A solution of *cis*-bis(triethylphosphine)dimethylplatinum (0·42 g.) in dry ether (8 c.c.) was treated with hydrogen chloride in dry ether (2·00 c.c.; 0·461N; 1 mol.). Almost immediately, colourless crystals separated. The mixture was evaporated to dryness, and the residue digested with light petroleum (b. p. <40°), leaving *cis*-bis(triethylphosphine)chloro(methyl)platinum (0·43 g.), m. p. 112—120° (decomp.). On recrystallisation from light petroleum (b. p. 60—100°) it formed long colourless needles, m. p. 114—119° (decomp.).

Attempts to prepare cis-*Bis(triethylphosphine)chloro(methyl)platinum* $[(PEt_3)_2PtMeCl]$.—(1) *By action of methyl-lithium* (1 *mol.*) *on* cis-*bis(triethylphosphine)dichloroplatinum. cis*-Bis(triethylphosphine)dichloroplatinum (1·50 g.) in boiling benzene (175 c.c.) under nitrogen was treated with methyl-lithium in ether (10·0 c.c.; 0·33N). Lithium chloride was filtered off and the filtrate, on cooling, deposited unchanged *cis*-bis(triethylphosphine)dichloroplatinum (0·25 g.). The colourless mother-liquor was evaporated and the residue dissolved in hot light petroleum (b. p. 80—100°). On cooling, *cis*-bis(triethylphosphine)chloro(methyl)platinum (0·03 g.) separated which recrystallised from light petroleum (b. p. 80—100°) in needles, m. p. and mixed m. p. 110—113° (decomp.). The original petroleum mother-liquors, on evaporation, yielded *cis*-bis(triethylphosphine)dimethylplatinum (0·49 g.), m. p. 78—81°.

(2) *By fission of* cis-*bis(triethylphosphine)dimethylplatinum with excess of hydrogen chloride.* A solution of *cis*-bis(triethylphosphine)dimethylplatinum (0·40 g.) in light petroleum (15 c.c.; b. p. <40°) was treated with an excess of dry hydrogen chloride at 0° for 30 seconds. Almost immediately a colourless precipitate was formed. The suspension was extracted repeatedly

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with light petroleum (b. p. 60—100°). This extract, on cooling to 0°, deposited *cis*-bis(triethylphosphine)chloro(methyl)platinum (0·11 g.) as long colourless needles, m. p. 116—119° (decomp.) (Found: C, 32·5; H, 7·0%). The petroleum-insoluble residue, on crystallisation from chloroform–light petroleum, gave *cis*-bis(triethylphosphine)dichloroplatinum (0·09 g.), m. p. 187—190°.

(3) *By isomerisation of* trans-*bis(triethylphosphine)chloro(methyl)platinum to the* cis-*isomer.* The *trans*-compound (0·24 g.) in light petroleum (b. p. 60—80°; 4 c.c.) and triethylphosphine (0·03 g.) were kept for 1 hr. at 25°. By this time colourless prisms, m. p. 96—99°, of the unchanged starting material had separated. After 2 weeks at 20° evaporation under reduced pressure gave a quantitative recovery of material, m. p. 93—99°, undepressed on admixture with the pure starting material, m. p. 99—100°. Very little *cis*-bis(triethylphosphine)chloro(methyl)platinum could have been formed.

Isomerisation of cis-*Bis(triethylphosphine)chloro(methyl)platinum to the* trans-*Isomer.*—The *cis*-compound (0·15 g.), suspended in light petroleum (b. p. 60—80°; 4 c.c.), was heated with triethylphosphine (0·01 g.), giving a homogeneous solution. This was cooled and evaporated to dryness, giving a colourless crystalline residue (0·15 g.), m. p. 95—100°, of *trans*-bis(triethylphosphine)chloro(methyl)platinum. Recrystallisation from methyl alcohol containing a little water gave the pure *trans*-isomer, m. p. 98—100°.

Attempts to prepare trans-*Bis(triethylphosphine)dimethylplatinum.*—(1) *From* cis-*bis(triethylphosphine)dimethylplatinum.* The *cis*-compound (0·1 g.) was heated at 130°/12 mm. and the distillate condensed on a cold finger placed *ca.* 1 cm. away. The solid distillate was collected at intervals, and heating was continued until no more distilled (a black residue remained) (yield 0·04 g.; m. p. 50—78°). This distillate was chromatographed on alumina (10 g.); elution with light petroleum (b. p. <40°) containing 20% of ether gave substantially pure trans-*bis(triethylphosphine)dimethylplatinum*, as colourless needles, m. p. 76—79° (0·012 g.) (Found: C, 36·75; H, 7·9. $C_{14}H_{36}P_2Pt$ requires C, 36·45; H, 7·85%). The mixed m. p. with the *cis*-isomer was 55—81°.

(2) *From* trans-*bis(triethylphosphine)dibromoplatinum.* Methylmagnesium bromide was prepared from magnesium (0·48 g.), ether (20 c.c.), and methyl bromide. Benzene (30 c.c.) was added and most of the ether was distilled off (temperature of vapour 65°). *trans*-Bis(triethylphosphine)dibromoplatinum (1·2 g.) was added, and the mixture heated under reflux for 1½ hr. After hydrolysis with ice and hydrochloric acid isolation in the usual way gave a product which, after four crystallisations from methyl alcohol, afforded *cis*-bis(triethylphosphine)dimethylplatinum as colourless prisms (0·42 g.), m. p. 80—81° (Found: C, 36·5; H, 7·85%).

(3) *By action of methyl-lithium* (2·2 *mol.*) *on* trans-*bis(triethylphosphine)dichloroplatinum. trans*-Bis(triethylphosphine)dichloroplatinum (1·00 g.) in dry ether (15 c.c.) and benzene (15 c.c.) was treated with a solution of methyl-lithium (10 c.c.; 0·445N; 2·2 mol.). The solution became colourless at once and lithium chloride was precipitated. After evaporation to dryness the residue was extracted with hot light petroleum (b. p. 60—80°), and the filtrate evaporated to dryness. After one crystallisation from methyl alcohol and one from light petroleum (b. p. 60—80°) this last residue gave *cis*-bis(triethylphosphine)dimethylplatinum (0·32 g.) as colourless prisms, m. p. 78—81°.

Bis(triphenylphosphine)iodo(methyl)platinum [$(PPh_3)_2PtMeI$].—Tris(triphenylphosphine)-platinum [17] was prepared by reduction of *cis*-[$(PPh_3)_2PtCl_2$] in alcoholic suspension in the presence of triphenylphosphine (1 mol.) with hydrazine hydrate (Found: C, 65·7; H, 4·7. Calc. for $C_{54}H_{45}P_3Pt$: C, 66·05; H, 4·6%). This (2·00 g.) in methyl iodide (18 c.c.) was kept for 1 hr. The solution gradually lightened and methyl(triphenyl)phosphonium iodide separated. The mixture was evaporated to dryness, and the residue boiled with methyl alcohol and filtered off. The insoluble portion, recrystallised from benzene, formed colourless prisms (1·2 g.) of *bis(triphenylphosphine)iodo(methyl)platinum* (Found: C, 51·4; H, 3·9. $C_{37}H_{33}IP_2Pt$ requires C, 51·6; H, 3·85%). With potassium thiocyanate in boiling acetone this iodide was converted into the *thiocyanate*, *trans*-[$(PPh_3)_2PtMe(SCN)$], which formed colourless prisms from benzene–methyl alcohol (Found: C, 57·55; H, 4·35. $C_{38}H_{33}NSP_2Pt$ requires C, 57·55; H, 4·2%).

Metathetical Replacements.—(1) trans-*Bis(triethylphosphine)bromo(methyl)platinum from the chloride. trans*-Bis(triethylphosphine)chloro(methyl)platinum (0·13 g.) in acetone (12 c.c.) was heated under reflux with lithium bromide (1·0 g.) for ½ hr. The acetone was removed under reduced pressure and the water-insoluble residue crystallised twice from methyl alcohol,

to give *trans*-bis(triethylphosphine)bromo(methyl)platinum (0·085 g.) (Found: C, 29·7; H, 6·3%).

(2) trans-*Bis(triethylphosphine)iodo(methyl)platinum from the chloride.* A solution of the chloride (0·12 g.) and sodium iodide (0·250 g.) in acetone (5 c.c.) was put aside for 1 hr. After evaporation the residue was washed with water, to give *trans*-bis(triethylphosphine)iodo-(methyl)platinum (0·135 g.), m. p. 70—70·5° without recrystallisation.

(3) trans-*Bis(triethylphosphine)methyl(thiocyanato)platinum* [$(PEt_3)_2PtMe(SCN)$] *from the iodide.* The iodo-complex (0·350 g.) in acetone (20 c.c.) was heated with potassium thiocyanate (1·0 g.) under reflux for 90 min. Evaporation and isolation of the water-insoluble portion afforded the trans-(*thiocyanato-compound* (0·210 g.) as needles [from light petroleum (b. p. 80—100°)] (Found: C, 33·2; H, 6·5; N, 3·1. $C_{14}H_{33}NSP_2Pt$ requires C, 33·3; H, 6·6; N, 2·8%).

(4) trans-*Bis(triethylphosphine)methyl(nitrato)platinum* [$(PEt_3)_2PtMe(NO_3)$] *from the iodide.* A solution of the *trans*-iodide (0·530 g.) in methyl alcohol (25 c.c.) was treated with silver nitrate (0·170 g.) in aqueous methyl alcohol [methyl alcohol (10 c.c.), water (5 c.c.)]. Silver iodide was precipitated at once but there was also some reduction to metallic silver. The precipitate was filtered off and the solution evaporated to dryness, giving a solid residue which on crystallisation from light petroleum (b. p. 60—80°) yielded trans-*bis(triethylphosphine)-methyl(nitrato)platinum* (0·33 g.) as colourless needles (Found: C, 31·0; H, 6·7; N, 2·7. $C_{13}H_{33}O_3NP_2Pt$ requires C, 30·7; H, 6·5; N, 2·8%). In 0·137% w/v nitrobenzene solution at 19° the nitrate had a molar conductivity of 1·41 mho.

Fission Reactions.—(1)*Iodine and* cis-*bis(triethylphosphine)dimethylplatinum.* To a solution of bis(triethylphosphine)dimethylplatinum (0·273 g.) in benzene (10 c.c.) was added iodine (0·127 g.) in benzene (10 c.c.) with vigorous shaking. The iodine colour was discharged rapidly, the solution becoming pale orange. Removal of the benzene under reduced pressure and crystallisation of the residue from methyl alcohol afforded *trans*-bis(triethylphosphine)iodo-(methyl)platinum (0·260 g.), m. p. and mixed m. p. 71—71·5° (Found: C, 27·5; H, 5·7%).

(2) *Iodine and* trans-*bis(triethylphosphine)iodo(methyl)platinum.* The complex (0·563 g.) was treated in benzene (10 c.c.) with iodine (0·254 g.) in benzene (10 c.c.), with shaking. The colour of the iodine was discharged rapidly. Evaporation of the solution and crystallisation of the residue from methyl alcohol afforded *trans*-bis(triethylphosphine)di-iodoplatinum (0·510 g.), m. p. 136·5—137·5°.

(3) *Magnesium iodide and bis(triphenylphosphine)dimethylplatinum.* A solution of magnesium iodide in ether was prepared from magnesium (excess), iodine (3·0 g.), and ether (40 c.c.). This was added to the dimethylplatinum complex (0·30 g.) in benzene (15 c.c.), and the mixture heated under reflux for 3 hr., then kept at 20° for 16 hr. Bis(triphenylphosphine)iodo(methyl)-platinum separated (0·29 g.), having m. p. 267—270° (decomp.). This iodide is identical with that prepared from tris(triphenylphosphine)platinum(0) (mixed m. p., infrared spectra, and identical thiocyanate produced on treatment with potassium thiocyanate).

(4) *Magnesium iodide and* cis-*bis(triethylphosphine)dimethylplatinum.* A solution of magnesium iodide, from iodine (0·40 g.), ether (25 c.c.), and excess of magnesium, was decanted from excess of magnesium, and *cis*-bis(triethylphosphine)dimethylplatinum (0·15 g.) was added. A white precipitate was formed rapidly. After 1 hr. at 20° the mixture was poured on ice and dilute hydrochloric acid. The ether layer was dried and evaporated. The residue recrystallised from methyl alcohol, giving *trans*-bis(triethylphosphine)di-iodoplatinum (0·11 g.), m. p. 135—136°. Dilution of the mother-liquors with water gave a cream precipitate which, recrystallised from aqueous methyl alcohol, gave *trans*-bis(triethylphosphine)iodo(methyl)platinum, m. p. 70—71°.

Reaction between cis-*Bis(triethylphosphine)dimethylplatinum and* cis-*Bis(triethylphosphine)-dichloroplatinum.*—A mixture of *cis*-bis(triethylphosphine)dimethylplatinum (0·461 g., 0·001 mole) and *cis*-bis(triethylphosphine)dichloroplatinum (0·502 g., 0·001 mole) was heated under reflux in benzene (10 c.c.) for 12 min. The pale yellow solution was evaporated to dryness and the residue extracted with hot light petroleum (b. p. 80—100°). The undissolved residue (small) was unchanged *cis*-bis(triethylphosphine)dichloroplatinum. The petroleum extract, on cooling to 0°, deposited *trans*-bis(triethylphosphine)dichloroplatinum (0·22 g.). The mother-liquors on evaporation under reduced pressure gave a mixture of colourless needles and colourless prisms which were separated by hand-picking and shown to be *trans*-bis(triethyl-phosphine)chloro(methyl)platinum, m. p. 93—98°, and *cis*-bis(triethylphosphine)dimethyl-platinum, m. p. 78—81°, respectively.

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TABLE 2. *Dipole moments of methylplatinum complexes in benzene at 25°*

$10^3\omega$	$\Delta\varepsilon/\omega$	$10^3\Delta n/\omega$	$-\Delta v/\omega$	$_TP$	$_EP$	$_OP$	$\mu(\pm 0{\cdot}1$ D)
			cis-$(PEt_3)_2PtMe_2$				
5·422	7·562	—	—	—	—	—	—
6·133	7·558	—	—	—	—	—	—
6·461	7·521	—	—	—	—	—	—
25·10	—	—	0·466	—	—	—	—
33·96	—	—	0·477	—	—	—	—
42·00	—	4·143	—	—	—	—	—
63·39	—	4·297	—	741·10	93·71	633·33	5·55
			trans-$(PEt_3)_2PtMeI$				
2·851	3·521	—	—	—	—	—	—
3·462	3·509	—	—	—	—	—	—
4·085	3·551	—	—	—	—	—	—
24·63	—	—	0·601	—	—	—	—
34·92	—	—	0·624	—	—	—	—
24·92	—	5·899	—	—	—	—	—
38·95	—	5·912	—	—	—	—	—
55·51	—	5·912	—	—	—	—	—
73·73	—	5·934	—	472·28	109·36	346·52	4·1
			trans-$(PEt_3)_2PtMeBr$				
2·525	3·103	—	—	—	—	—	—
—	—	—	(0·57)	398 *	(101)	282 *	3·7 *
			trans-$(PEt_3)_2PtMeCl$				
5·610	2·947	—	—	—	—	—	—
5·352	2·865	—	—	—	—	—	—
1·673	2·904	—	—	—	—	—	—
16·79	—	—	0·524	—	—	—	—
15·78	—	—	0·532	—	—	—	—
21·92	—	3·963	—	—	—	—	—
52·83	—	4·154	—	—	—	—	—
61·66	—	4·002	—	352·50	98·46	239·06	3·4
			cis-$(PEt_3)_2PtMeCl$				
3·792	16·264	—	—	—	—	—	—
4·513	16·157	—	—	—	—	—	—
5·621	16·233	—	(0·53)	1561 *	(98)	1447 *	8·4 *
			trans-$(PEt_3)_2Pt(Me)SCN$				
2·660	9·941	—	—	—	—	—	—
6·745	—	—	0·474	—	—	—	—
14·77	—	6·107	—	—	—	—	—
29·61	—	6·220	—	1045·86	117·24	911·03	6·65
6·926	7·940	—	*trans*-$(PEt_3)_2Pt(Me)NO_2$ (0·48)	862 *	(101)	745 *	6·05 *
3·657	2·993	—	*trans*-$(PPr^n_3)_2PtMeI$ (0·650)	468 *	(137)	310 *	3·9 *
			cis-$(PPh_3)_2PtMe_2$				
2·919	4·770	—	—	—	—	—	—
4·321	4·877	—	—	—	—	—	—
5·252	4·832	—	—	—	—	—	—
7·866	—	—	0·509	—	—	—	—
8·743	—	—	0·515	—	—	—	—
12·88	—	11·89	—	—	—	—	—
13·00	—	12·03	—	823·45	190·88	603·94	5·45
			trans-$(PPh_3)_2Pt(Me)SCN$				
2·141	6·420	—	(0·52)	1108 *	(208)	869 *	6·5 *
			$(Et_2P{\cdot}CH_2{\cdot}CH_2{\cdot}PEt_2)PtMe_2$				
7·979	11·316	—	—	—	—	—	—
8·491	11·377	—	—	—	—	—	—
8·955	11·410	—	(0·47)	1011 *	(82)	916 *	6·7 *
			$(PEt_3)_2PtMe_2I_2$				
5·964	5·643	—	—	—	—	—	—
6·016	5·619	—	—	—	—	—	—
6·629	5·570	—	—	—	—	—	—
7·766	5·651	—	—	—	—	—	—
12·14	—	—	0·675	—	—	—	—
38·49	—	—	0·665	—	—	—	—
24·62	—	9·037	—	—	—	—	—
30·74	—	9·007	—	858·92	136·76	701·65	5·85
5·399	6·040	—	$(PEt_3)_2PtMe_2Cl_2$ (0·58)	696 *	(110)	569 *	5·3 *
3·909	4·928	—	$(PPr^n_3)_2PtMe_2I_2$ (0·69)	851 *	(165)	686 *	5·8 *
4·568	14·739	—	$(EtS{\cdot}CH_2{\cdot}CH_2{\cdot}SEt)PtMe_2$ (0·57)	1107 *	(61)	1037 *	7·1 *

* Calculated by using estimated values of densities and refractivities. Estimated values are given in parentheses. Those of $-\Delta v/\omega$ are needed only approximately and were estimated from experience of measurements on similar compounds. Those of $_EP$ were estimated by using group refractivities (Vogel, *J.*, 1948, 1833 and references therein) and from our measured values for other similar compounds.

Reaction between cis-*Bis(triethylphosphine)dimethylplatinum and* cis-*Bis(triethylphosphine)-dichloroplatinum in the Presence of Dichlorobis(triethylphosphine)-μμ′-dichlorodiplatinum.*—A mixture of *cis*-bis(triethylphosphine)dichloroplatinum (0·460 g.), *cis*-bis(triethylphosphine)-dimethylplatinum (0·461 g.) and dichlorobis(triethylphosphine)-μμ′-dichlorodiplatinum (0·020 g.) was heated under reflux in benzene (15 c.c.) for 30 min. A pale brown solution was formed which, on cooling, deposited unchanged *cis*-bis(triethylphosphine)dichloroplatinum (0·35 g.), m. p. 185—191°. The mother-liquors were evaporated to dryness and the residue was extracted with boiling light petroleum (b. p. <40°). This extract on evaporation gave a mixture of needles and prisms (0·35 g.), m. p. 60—78°, from which *cis*-bis(triethylphosphine)-dimethylplatinum was isolated by repeated recrystallisation from light petroleum (b. p. 40—60°) [*trans*-bis(triethylphosphine)chloro(methyl)platinum was also probably present]. The residue from the light petroleum (b. p. <40°) extraction was re-extracted with light petroleum (b. p. 60—100°), leaving a small residue of *cis*-bis(triethylphosphine)dichloroplatinum. The petroleum (b. p. 60—100°) extract, on cooling to 0°, deposited *cis*-bis(triethylphosphine)chloro(methyl)-platinum (0·008 g.), m. p. and mixed m. p. 110—113° (decomp.).

Addition Reactions.—(1) *Methyl iodide to bis(trialkylphosphine)iodo(methyl)platinum.* *trans*-Bis(triethylphosphine)iodo(methyl)platinum (2·00 g.) was heated with methyl iodide (10 c.c.) in a sealed tube at 100° for 1 hr. Evaporation of the methyl iodide and recrystallisation of the residue from benzene–light petroleum (b. p. 60—80°) gave bis(triethylphosphine)di-iodo-(dimethyl)platinum [$(PEt_3)_2PtMe_2I_2$] (1·65 g.) as colourless needles (Found: C, 23·65; H, 5·1. $C_{14}H_{36}I_2Pt$ requires C, 23·5; H, 5·05%). After this compound had been heated for 3 hr. at 80°/0·01 mm., *trans*-bis(triethylphosphine)iodo(methyl)platinum, m. p. 70—71° was recovered quantitatively.

Bis(tri-n-propylphosphine)di-iodo(dimethyl)platinum [$(PPr_3)_2PtMe_2I_2$] was similarly prepared from *trans*-bis(tripropylphosphine)iodo(methyl)platinum in 69% yield as colourless needles from light petroleum (b. p. 80—100°) (Found: C, 30·4, 30·4; H, 6·0, 5·7. $C_{20}H_{48}I_2P_2Pt$ requires C 30·0; H, 6·1%).

(2) *Chlorine to* cis-*bis(triethylphosphine)dimethylplatinum* The complex (0·461 g., 0·001 mole) in benzene (5 c.c.) was treated with a solution of chlorine (0·071 g., 0·001 mole) in carbon tetrachloride (2·3 c.c.). The solution was evaporated to dryness and the residue recrystallised from methyl alcohol and then light petroleum (b. p. 80—100°), giving *bis(triethylphosphine)-dichloro(dimethyl)platinum* [$(PEt_3)_2PtMe_2Cl_2$] (0·32 g.) as colourless plates (Found: C, 31·7; H, 6·8; Cl, 12·8. $C_{14}H_{36}Cl_2P_2Pt$ requires C, 31·6; H, 6·8; Cl, 13·3%).

Action of Iodine on Bis(triethylphosphine)di-iodo(dimethyl)platinum.—The di-iodo-complex (0·238 g.) was treated in benzene (15 c.c.) with iodine (0·086 g.) in benzene (10 c.c.). The colour persisted for 1 hr. but disappeared after 15 min. under reflux. Removal of the benzene under reduced pressure and crystallisation of the residue from methyl alcohol gave bis(triethyl-phosphine)di-iodoplatinum (0·23 g.), m. p. 135—137°.

Determination of Dipole Moments.—Dielectric constants (ε) were measured with a heterodyne beat capacity meter based on that of Hill and Sutton,[22] and a glass cell, of about 9 c.c. liquid capacity and 33·52 μμF electrical capacity, based on that manufactured by Kipp of Delft. The refractive indices (n) were determined with a Pulfrich refractometer and specific volumes (v) with the usual U-shaped pyknometer. The dipole moments were evaluated by the method of Everard, Hill, and Sutton.[23] It was assumed, however, that the atom polarisation ($_AP$) is equal to 15% of the electron polarisation ($_EP$) and that $_EP$ is equal to the molar refractivity for the red helium line (6678·1 Å). The measurements are recorded in Table 2. ω is the weight fraction of solute, $\Delta\varepsilon = \varepsilon_S - \varepsilon_B$, where ε_S = dielectric constant of solution, ε_B = dielectric constant of benzene, and similarly for Δn and Δv. Measurements refer to benzene solution at 25°. The value ε_B 2·2727 was used to calibrate the capacity meter.[24]

The authors thank Dr. L. E. Orgel for useful discussion, Mr. P. F. Todd and Miss I. Bates for measuring the dipole moments, and Messrs. A. E. Field, C. J. Pembroke and M. L. Searle for other experimental assistance.

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[22] Cf. Everard and Sutton, *J.*, 1949, 2313.
[23] Everard, Hill, and Sutton, *Trans. Faraday Soc.*, 1950, **46**, 417.
[24] Hartshorn and Oliver, *Proc. Roy. Soc.*, 1929, *A*, **123**, 683.

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142. *The Interaction of Hexamethyldisiloxane with Aluminium Halides and with Iodine.*

By Alan H. Cowley, Fred Fairbrother, and Norman Scott.

Aluminium chloride and bromide do not form stable adducts with hexamethyldisiloxane, but cleavage of a silicon–oxygen bond occurs with formation of trimethylmonohalogenosilanes and trimethylsiloxyaluminium dihalides. The latter are stable crystalline compounds at room temperature: the dichloride melts at 87—88° and can be distilled *in vacuo*. Both dihalides undergo disproportionation on further heating, into trimethylhalogenosilanes and aluminium oxyhalide.

Iodine forms a purple solution in hexamethyldisiloxane, which behaves as a non-donor solvent.

Emeléus and his co-workers have shown [1] that the electron-donor activity of oxygen and sulphur in dialkyl ethers is absent in their disilyl analogues and that when boron trifluoride or trichloride reacts with 1 : 1′-dimethyl-, 1 : 1′ : 2 : 2′-tetramethyl-, or hexamethyldisiloxane, no stable adduct is formed but cleavage of the Si–O–Si bond occurs, with formation of the methylhalogenosilane and the methylsiloxyboron dihalide. The latter decomposes spontaneously to the methylhalogenosilane, boron trihalide, and boron trioxide.

We have found that a somewhat similar reaction, $(Me_3Si)_2O + \frac{1}{2}Al_2Cl_6 = Me_3SiCl + Me_3Si{\cdot}O{\cdot}AlCl_2$, occurs between hexamethyldisiloxane and aluminium chloride, and correspondingly for the bromide. No stable adduct is formed, but the corresponding trimethylsiloxyaluminium dihalides are much more stable than the boron analogues. The chloride, in particular, forms well-defined crystals and can be distilled in a good vacuum without decomposition: heating under atmospheric pressure, however, leads to decomposition into trimethylchlorosilane and aluminium oxychloride. The bromide is less stable than the chloride: the crystals do not melt, but decompose at 100° into trimethylbromosilane and aluminium oxybromide.

Experimental

A commercial "Silicone Fluid : 0·65 centipoise," which was almost pure hexamethyldisiloxane, was dried (P_2O_5) and fractionated: b. p. 100·3°/768 mm. Aluminium chloride and bromide were prepared from high-purity aluminium wire and hydrogen chloride and bromine, respectively. Both halides were purified by five or six vacuum-sublimations and stored in sealed ampoules.

Reaction of aluminium chloride. An ampoule containing about 15 g. was opened under dry nitrogen and transferred to 50 c.c. of hexamethyldisiloxane. Several hours' shaking at room temperature produced little dissolution. The flask containing the mixture was then immersed in a bath at 40° and shaken occasionally: complete dissolution occurred within ¾ hr. On cooling and storage overnight, large (*ca.* several mm.) thin plates were deposited. The mother-liquor was decanted and the crystals were dried *in vacuo* [Found: H, 4·8; C, 19·4; Al, 14·7; Cl, 38·2. $Me_3Si{\cdot}O{\cdot}AlCl_2$ requires H, 4·8; C, 19·3; Al, 14·3; Cl, 38·0%]. Fractionation of the mother-liquor gave, in addition to unchanged hexamethyldisiloxane, a major fraction consisting of trimethylchlorosilane, b. p. 57·2°/764 mm. [Found: H, 8·5; C, 33·1; Cl, 32·9. Calc. for Me_3SiCl: H, 8·4; C, 33·2; Cl, 32·7%].

The crystals of $Me_3Si{\cdot}O{\cdot}AlCl_2$ were quite stable at room temperature and when sealed in an evacuated tube melted at 87—88° and could be distilled from end to end of the tube at about 145—150°. In air, hydrolysis occurred rapidly and the crystals disintegrated to a white powder. When they were heated at atmospheric pressure, decomposition occurred according to the equation

$$Me_3Si{\cdot}O{\cdot}AlCl_2 = Me_3SiCl + AlOCl$$

the trimethylchlorosilane distilling off and leaving a residue which was chiefly amorphous aluminium oxychloride (Found: Al, 31·0; Cl, 42·3. Calc. for AlOCl : Al, 33·9; Cl, 45·3%).

[1] Emeléus, MacDiarmid, and Maddock, *J. Inorg. Nuclear Chem.*, 1955, **1**, 194; Emeléus and Onyszchuk, *J.*, 1958, 604.

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This decomposition into trimethylchlorosilane and aluminium oxychloride rather than into aluminium oxide and chloride is in contrast to the reaction with boron halides.

Reaction of aluminium bromide. About 15 g. of the bromide were added to 50 c.c. of hexamethyldisiloxane. As there was an immediate exothermic reaction, the flask was cooled in ice and shaken until dissolution was complete. On removal of about one third of the liquid under vacuum, a crop of small (*ca.* 1 mm.) white crystals of $Me_3Si{\cdot}O{\cdot}AlBr_2$ was obtained [Found: H, 3·7; C, 11·9; Br, 56·7. $Me_3Si{\cdot}O{\cdot}AlBr_2$ requires H, 3·3; C, 13·0; Br, 57·9%].

The other reaction product was similarly identified as trimethylbromosilane. Failure to cool the mixture during dissolution led to immediate partial decomposition and no crystalline product was obtained.

The $Me_3Si{\cdot}O{\cdot}AlBr_2$ did not melt in an evacuated sealed tube, but decomposed at about 100° with evolution of trimethylbromosilane (b. p. 78°). The solid residue was aluminium oxybromide (Found: Al, 22·3; Br, 64·5. Calc. for AlOBr : Al, 22·0; Br, 65·0%). When the oxybromide was heated at 100° under vacuum for 2 hr., slight decomposition occurred, as indicated by a small white sublimate. At 180° and heating for a further 2 hr. this developed into a crystalline sublimate of aluminium bromide, indicating, as previously suggested,[2] that a disproportionation $6AlOBr \longrightarrow Al_2Br_6 + 2Al_2O_3$ takes place under these conditions. The disproportionation was not complete, much bromine being retained, probably mechanically, in the solid phase.

These reactions between hexamethyldisiloxane and aluminium halides provide a very convenient method for the preparation, from readily available materials and in good yield, of trimethyl-chloro- and -bromo-silanes, and also of nearly pure AlOBr.

The lack of donor activity of the oxygen atom in methyl-siloxanes has been attributed in part to the ability of the silicon atom to use the vacant 3*d* orbitals in the formation of π-type bonds with the oxygen.[1,5] Further evidence of this lack of donor activity is given by the behaviour of iodine in hexamethyldisiloxane. The colour of iodine solutions can [3] be correlated with the electron-donor character of the solvent, being purple, as in the vapour, in solvents such as carbon tetrachloride and hexane, and brown in donor solvents such as alcohols, ethers, esters, and olefins. We have also examined the absorption spectrum of iodine in hexamethyldisiloxane: the colour is purple, with a maximum $\varepsilon = 850$ at 518 mμ, which is very similar to that in carbon tetrachloride.[4]

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 15th*, 1958.]

[2] Fairbrother and Frith, *J.*, 1953, 2975.
[3] Fairbrother, *Nature*, 1947, **160**, 87; *J.*, 1948, 1051.
[4] Gmelin, "Handb. d. anorg. Chem.," [8], **8**, 116.
[5] Stone and Seyferth, *J. Inorg. Nuclear Chem.*, 1955, **1**, 112.

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143. *The Structure of the Fructosan from* Agave vera cruz *Mill.*

By G. O. ASPINALL and P. C. DAS GUPTA.

Fractionation of the fructosan from *Agave vera cruz* Mill gave fractions containing an average of one glucose residue per molecule. Hydrolysis of the methylated fructosan afforded 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, and 1 : 3 : 4 : 6-tetra-, 3 : 4 : 6-tri-, 1 : 3 : 4-tri-, and 3 : 4-di-*O*-methyl-D-fructose in the approximate molar ratio of 1 : 8 : 10 : 5 : 7. Evidence was obtained for sucrose as a product of partial acid-hydrolysis of the fructosan. The greater part of the material possesses, therefore, a molecular structure comprising a highly branched chain of *ca.* 30 2 : 1- and 2 : 6-linked β-D-fructofuranose residues terminated by a non-reducing D-glucopyranose residue as in sucrose.

FRUCTOSANS from plants [1] are characterised by chains of 2 : 1- and 2 : 6-linked β-D-fructofuranose residues, the former mode of linkage being typical of inulin and the latter typical of the grass levans. In addition to these essentially linear polysaccharides, highly branched

[1] Hirst, *Proc. Chem. Soc.*, 1957, 193.

fructosans containing both types of linkage have been encountered. Chemical investigations have shown that several of these fructosans contain within their molecular structure a sucrose moiety and it is probable that the polysaccharides are end-products of the transfructosylation by which the lower fructose-containing oligosaccharides are known to be synthesised from sucrose. A fructosan is the major carbohydrate constituent of the stem of *Agave vera cruz* Mill,[2] and we are grateful to Dr. M. Srinivasan for placing at our disposal a quantity of this material for structural investigation, the results of which are described in this paper.

The fructosan was fractionated by precipitation from aqueous solution with ethanol. Samples of the fractions were hydrolysed and the proportions of fructose and glucose formed were determined. Molecular-weight determinations, by the isothermal-distillation method, of the fructosan acetates indicated that the fractions contained series of polymer homologues, each fructosan molecule containing on the average one glucose residue. The negative optical rotations of the fructosan acetates ($[\alpha]_D$ $-16{\cdot}5°$ to $-9°$) suggested that the fructosan approximated to the inulin rather than to the levan type.[3] Periodate oxidation indicated the consumption of $n + 1$ moles of reagent per molecule of n hexose residues with the liberation of one mole of formic acid per mole of fructosan. Since no sugar residues remained unattacked by the reagent, it is possible that each fructose residue consumed one mole of periodate, whilst the glucose residue consumed two moles of reagent with release of formic acid. The largest polysaccharide fraction was then selected for more detailed study.

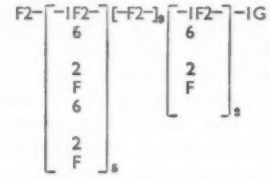
The fructosan was converted into its fully methylated derivative which had a number-average molecular weight of 6300 ± 500 (degree of polymerisation, 31 ± 2). Hydrolysis of the methylated polysaccharide gave a mixture of sugars from which three fractions containing tetra-, tri-, and di-*O*-methylhexose were obtained after chromatography on cellulose. The first fraction contained 1 : 3 : 4 : 6-tetra-*O*-methyl-D-fructose (27%) and 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose (2·65%), and the sugars were separated chromatographically after preferential conversion of the former sugar into its methyl glycoside.[4] The second fraction contained a mixture of 3 : 4 : 6- (33%) and 1 : 3 : 4-tri-*O*-methyl-D-fructose (16%), and separation of these two sugars was effected after conversion of the former into its *O*-*iso*propylidene derivative.[5] The third fraction contained 3 : 4-di-*O*-methyl-D-fructose. The five methylated sugars isolated on hydrolysis of the methylated fructosans were obtained in an approximate molar ratio of 8 : 1 : 10 : 5 : 7.

It follows that the fructosan from *Agave vera cruz* Mill is a highly branched polysaccharide in which both 2 : 1- and 2 : 6-linked β-D-fructofuranose residues are present. D-Glucose residues are present solely as non-reducing end groups and must therefore be an integral part of the fructosan molecule. The quantity of tetra-*O*-methyl-D-glucose isolated on hydrolysis of the methylated polysaccharide indicated that each fructosan molecule contained one such glucose residue. Further evidence for the nature of the glucose residues came from the isolation of a disaccharide, identified as sucrose by chromatography and by hydrolysis to glucose and fructose, as a product of partial acid-hydrolysis of the polysaccharide. It follows that the branched fructosan molecules are terminated by non-reducing D-glucopyranose residues linked as in sucrose. Sucrose has been similarly isolated previously from perennial ryegrass levan [6] and from inulin.[7]

These results show that this polysaccharide belongs to the same general family as other plant fructosans.[1] It most closely resembles triticin from couch grass [8] and the fructosan from the Hawaian Ti plant,[5b] but differs from the latter polysaccharide in containing

[2] Srinivasan and Bhatia, *Biochem. J.*, 1953, **55**, 286.
[3] Schlubach and Sinh, *Annalen*, 1940, **544**, 111.
[4] R. Montgomery and Smith, *J. Amer. Chem. Soc.*, 1957, **79**, 446.
[5] (*a*) E. M. Montgomery, *ibid.*, 1934, **56**, 419; (*b*) Boggs and Smith, *ibid.*, 1956, **78**, 1880.
[6] Aspinall and Telfer, *J.*, 1955, 1106.
[7] Feingold and Avigad, *Biochim. Biophys. Acta*, 1956, **22**, 196; Holzer, Wittmann-Zinke, and Zinke, *Monatsh.*, 1957, **88**, 268.
[8] Arni and Percival, *J.*, 1951, 1822.

glucose residues as non-reducing end-groups rather than in the middle of the molecule. A unique structure cannot be advanced for the fructosan since methods are not yet available to indicate the distribution of 2 : 1- and 2 : 6-linkages in such branched polysaccharides, but the following structure is one of several possibilities. As this highly branched fructosan, like perennial ryegrass levan and inulin, contains a sucrose moiety, the recent isolation of the branched tetrasaccharide, bis-(2 ⟶ 1_F, 2 ⟶ 6_F)-*O*-D-fructofuranosylsucrose, from rye stems [9] is of particular interest since this is the simplest branched oligosaccharide in which both the linkages characteristic of fructosans are present.



F = D-fructofuranose and G = D-glucopyranose residues.

Experimental

Paper partition chromatography was carried out on Whatman No. 1 filter paper with the following solvent systems (v/v): (A) butan-1-ol–ethanol–water (4 : 1 : 5, upper layer); (B) ethyl acetate–acetic acid–water (3 : 1 : 3, upper layer); (C) butan-2-one, saturated with water; (D) light petroleum (b. p. 60—80°)–butan-2-one (1 : 1), saturated with water; (E) butan-1-ol–benzene–pyridine–water (5 : 1 : 3 : 3, upper layer). Paper ionophoresis was in borate buffer at pH 10.

Number-average molecular weights of acetylated and methylated polysaccharides were determined in benzene solution by the isothermal-distillation method.[10]

The fructosan was received as a white crystalline substance, $[\alpha]_D^{20}$ −34° (*c* 1·6 in H_2O) (Found: ash, 0·9%). Hydrolysis of a sample gave fructose and glucose in the proportion of 20 : 1.

Fractionation of Fructosan.—Fructosan (25·7 g.) was dissolved in water (325 ml.) and fractionation was effected by gradual addition of ethanol. The precipitated gels were dried after thorough washing with acetone. Samples (100 mg.) were hydrolysed in aqueous 1% oxalic acid (10 ml.) at 75° for 1·5 hr. After neutralisation with calcium carbonate, the hydrolysates were de-ionised with Amberlite resins IR-120(H) and IR-4B(OH), and the proportions of fructose and glucose were estimated by quantitative paper chromatography [11] with solvent B. Samples were acetylated in formamide by acetic anhydride and pyridine at 0° for 3 days. The acetylated polysaccharides were isolated by pouring the reaction mixture into water and were purifed by precipitation with light petroleum from chloroform solution. The following results were obtained:

Fraction	EtOH (%) in precipitant	Wt. (g.)	$[\alpha]_D$ (H_2O)	Fructose : glucose in hydrolysate	Acetylated fructosan $[\alpha]_D$ ($CHCl_3$)	Acetylated fructosan DP_n
1	75	0·5	—	—	—	—
2	82	16·9	−38°	34 : 1	−16·5°	32
3	88	4·0	−35°	20 : 1	−14°	18
4	91	0·8	−32·5°	16 : 1	−10°	16
5	Residue not ppted.	3·1	−24°	8 : 1	−9°	15 *

* The low yield of this sample of acetylated fructosan probably resulted in the recovery of the higher-molecular part of the fraction.

Periodate Oxidation.—Fructosan samples (250 mg.) were dissolved in water (30 ml.) and 0·25M-sodium metaperiodate (20 ml.) was added. The uptake of periodate, determined by the arsenite method, was constant after 43 hr. at values of 1·03, 1·06, 1·16, and 1·36 moles of periodate consumed per hexose residue for fractions 2—5 respectively. No sugars were detected on hydrolysis of periodate-oxidised fructosan (fraction 2).

[9] Schlubach and Koehn, *Annalen*, 1958, **614**, 126.
[10] Gee, *Trans. Faraday Soc.*, 1940, **36**, 1162.
[11] Flood, Hirst, and Jones, *J.*, 1948, 1679.

Oxidation of samples with potassium metaperiodate gave the following results (expressed as the number of hexose residues per mole of formic acid liberated) (constant after 216 hr.): 34, 23, 18, and 6 for fractions 2—5 respectively.

Methylation of Fructosan.—Fructosan (fraction 2, 6·2 g.) was methylated by successive additions of methyl sulphate and sodium hydroxide and then with methyl iodide and silver oxide to give methylated fructosan (4·8 g.), $[\alpha]_D$ −53·5° (*c* 1·3 in $CHCl_3$) (Found: OMe, 45·6%; DP_n, 31).

Methylated fructosan (3·2 g.) was refluxed with methanol (120 ml.) and water (40 ml.) containing oxalic acid (2 g.) for 22 hr. {$[\alpha]_D$ −56° ⟶ +30·5° (const.)}. The solution was concentrated to remove methanol, water (136 ml.) containing oxalic acid (1·2 g.) was added to the resulting solution, and the mixture was heated at 80° for 1·5 hr. ($[\alpha]_D$ +34° ⟶ +5·5°). The cooled solution was neutralised with calcium carbonate, filtered and concentrated to a syrup. Paper chromatograms run in solvent A and sprayed with aniline oxalate and urea oxalate for aldoses and ketoses showed tetra-*O*-methylglucose, and tetra-, tri-, and di-*O*-methylfructoses. Chromatography in solvent C showed two tri-*O*-methylfructoses. The syrupy mixture of sugars was separated on cellulose (60 × 3·5 cm.) with solvent C, to give three fractions.

Fraction 1. After careful removal of organic solvent by evaporation with water, the syrup was diluted with water to 100 ml. Chromatography showed 1 : 3 : 4 : 6-tetra-*O*-methylfructose and 2 : 3 : 4 : 6-tetra-*O*-methylglucose, and estimation of ketose colorimetrically[8] and of aldose by alkaline hypoiodite showed the two sugars to be present in the fraction to the extent of 990 mg. and 97 mg. respectively. After removal of water, the syrupy mixture of sugars was treated with methanolic 0·5% hydrogen chloride (80 ml.) at room temperature for 8 hr. to effect preferential methyl glycoside formation of the fructose derivative.[4] After neutralisation and removal of methanol the mixture was separated on cellulose (60 × 1·7 cm.) with solvent D, to give fractions 1*a* and 1*b*. Hydrolysis of fraction 1*a* with 0·2N-sulphuric acid (20 ml.) and methanol (7·5 ml.) on a boiling-water bath for 6 hr. furnished 1 : 3 : 4 : 6-tetra-*O*-methyl-D-fructose (642 mg.), $[\alpha]_D^{18}$ +32·8° (*c* 1·2 in H_2O) (Found: OMe, 52·8. Calc. for $C_{10}H_{20}O_6$: OMe, 52·5%), which was characterised by conversion into methyl 3 : 4 : 6-tri-*O*-methyl-D-fructofuranosiduronamide, m. p. 98—99°, $[\alpha]_D^{18}$ −71° (*c* 1·3 in H_2O). Fraction 1*b* (69 mg.) was identified as 2 : 3 : 4 : 6-tetra-*O*-methyl-D-glucose, m. p. and mixed m. p. 78—84°, $[\alpha]_D^{18}$ +87° (equil.) (*c* 0·8 in H_2O) (Found: OMe, 52·1. Calc. for $C_{20}H_{10}O_6$: OMe, 52·5%).

Fraction 2. Chromatography of the syrup (1·657 g.) in solvent C showed 1 : 3 : 4- and 3 : 4 : 6-tri-*O*-methylfructose. In order to convert the 3 : 4 : 6-trimethyl ether into the *O-iso*propylidene derivative,[5] the syrup (1·32 g.) was kept in acetone (25 ml.) containing concentrated sulphuric acid (0·15 ml.) at −20° for 48 hr. The solution was neutralised with sodium carbonate, filtered, and concentrated to a syrup which was separated on cellulose (60 × 3·5 cm.) with solvent C to give fractions 2*a* and 2*b*. Fraction 2*a* containing the *O-iso*propylidene derivative was hydrolysed with 2·25% oxalic acid (25 ml.) at 80° for 2 hr. to furnish 3 : 4 : 6-tri-*O*-methyl-D-fructose (715 mg.), $[\alpha]_D^{18}$ +21·3° (*c* 2·0 in $CHCl_3$) (Found: OMe, 42·0. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). The sugar was characterised by oxidation with lead tetra-acetate (cf. Lindberg and Wickberg [13]), followed by treatment of the derived lactone with methanolic ammonia, to give 2 : 3 : 5-tri-*O*-methyl-D-arabonamide, m. p. 136—137°, $[\alpha]_D^{18}$ −14·2° (*c* 2·1 in H_2O) (Found: OMe, 45·1. Calc. for $C_8H_{17}O_5N$: OMe, 44·9%). The *X*-ray powder photograph of the amide was identical with that of 2 : 3 : 5-tri-*O*-methyl-L-arabonamide. Fraction 2*b* (331 mg.) was chromatographically and ionophoretically pure and after recrystallisation from carbon tetrachloride–light petroleum (b. p. 40—60°) had m. p. and mixed m. p. (with 1 : 3 : 4-tri-*O*-methyl-D-fructose) 72—73° and $[\alpha]_D^{18}$ −50° (equil.) (*c* 1·0 in H_2O) (Found: OMe, 41·5. Calc. for $C_9H_{18}O_6$: OMe, 41·9%).

Fraction 3. The sugar (681 mg.), $[\alpha]_D^{18}$ −50·3° (*c* 1·0 in H_2O) (Found: OMe, 29·65. Calc. for $C_8H_{16}O_6$: OMe, 29·8%), was characterised as 3 : 4-di-*O*-methyl-D-fructose by conversion into methyl 3 : 4-di-*O*-methyl-D-fructofuranoside-1 : 6-dicarboxydiamide, m. p. 191° and $[\alpha]_D^{18}$ −68° (*c* 1·6 in H_2O) (Found: OMe, 37·6. Calc. for $C_9H_{16}O_6N_2$: OMe, 37·5%). The sugar was further identified by oxidation with lead tetra-acetate, followed by treatment of the derived lactone with methanolic ammonia, to give 2 : 3-di-*O*-methyl-D-arabonamide, m. p. 156—157°, $[\alpha]_D^{18}$ −13·6° (*c* 1·4 in H_2O) (Found: OMe, 32·3. Calc. for $C_7H_{15}O_5N$: OMe, 32·1%). The amide gave an *X*-ray powder photograph and an infrared spectrum identical with those of 2 : 3-di-*O*-methyl-L-arabonamide.

[13] Lindberg and Wickberg, *Acta Chem. Scand.*, 1953, **7**, 969.

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Hypoiodite Oxidation of Methylated Fructoses.—Estimation, by the hypoiodite method,[13] of the " aldose " content of fractions 2 and 3 gave values of 6·4 and 3·6%. Control experiments with synthetic samples of 3 : 4 : 6-tri- and 3 : 4-di-*O*-methyl-D-fructose gave values for apparent aldose content of 6·1 and 3·5%, whereas 1 : 3 : 4 : 6-tetra- and 1 : 3 : 4-tri-*O*-methyl-D-fructose gave values of 1·4 and 1·1%. The latter values probably arise from experimental error, but the larger values for apparent aldose content of D-fructose derivatives not containing a 1-substituent may arise from ketose–aldose interconversion under the alkaline conditions employed.

Partial Acid Hydrolysis of Fructosan.—The fructosan (unfractionated; 16 g.) was heated in water (800 ml.) containing oxalic acid (4 g.) at 75° for 15 min. The solution was neutralised with calcium carbonate, filtered, and concentrated to a syrup. Chromatography in solvent E showed fructose and a series of oligosaccharides. One of the components was chromatographically indistinguishable from sucrose and gave glucose and fructose on hydrolysis.

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[13] Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289.

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144. *Aliphatic Aldehydes in the Perkin Reaction.*

By MALCOLM CRAWFORD and W. T. LITTLE.

Under the conditions of the Perkin reaction aliphatic aldehydes give diacetates and enol acetates. When temperatures are low enough to suppress these reactions and the acid component is activated the Perkin reaction does take place with aliphatic aldehydes, except for the higher members. Comparison of the rates of reaction of a number of aliphatic and aromatic aldehydes with acetic anhydride and sodium *p*-nitrophenylacetate by a competitive method indicates that the reluctance of aliphatic aldehydes to undergo the Perkin reaction is due to the slowness of the elimination stage. Higher aliphatic aldehydes are unreactive because of a " rule of six " effect.

THE failure, long known, of aliphatic aldehydes to undergo the Perkin reaction has never been satisfactorily explained. Many carbonyl reactions such as semicarbazone formation [1] and addition of the Grignard reagent [2] take place more readily with aliphatic than with aromatic aldehydes. The same might be expected to apply to the Perkin reaction: certainly addition of the anion from the acid component, acetic anhydride, should take place less readily with aromatic than aliphatic aldehydes because of mesomeric spreading of the positive charge from the carbonyl group into the aromatic ring: [3] the non-reactivity of aliphatic aldehydes in the Perkin and related reactions has been vaguely attributed to competing reactions, such as aldol formation, which involve the α-hydrogen atoms.[4] The standard bath-temperature for the Perkin reaction is 180°. Few of the commoner aliphatic aldehydes would remain as liquids in the reaction flask at this temperature. Experiments in sealed tubes with pentanal,[5] heptanal,[5] and other aldehydes [6] have afforded minute quantities of the expected acids, but the higher, less volatile aldehydes have never been found to react under ordinary conditions. Semmler,[7] however,

[1] Conant and Bartlett, *J. Amer. Chem. Soc.*, 1932, **54**, 2881; Westheimer, *ibid.*, 1934, **56**, 1962.
[2] Kharasch and Cooper, *J. Org. Chem.*, 1945, **10**, 46.
[3] Dewar, " The Electronic Theory of Organic Chemistry," Oxford, 1949, p. 116.
[4] Carter, *Organic Reactions*, 1946, Vol. III, p. 208.
[5] Fittig and Schneegans, *Annalen*, 1885, **227**, 79.
[6] Kietreiber, *Monatsh.*, 1898, **19**, 735.
[7] Semmler, *Ber.*, 1909, **42**, 584, 1161, 2014.

has shown that many aliphatic aldehydes give diacetates and enol acetates in high yield when heated with acetic anhydride with or without sodium acetate. This side-reaction might account for the failure of the expected main reaction.

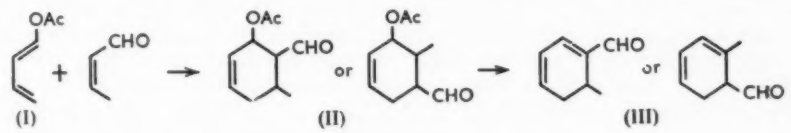
TABLE 1. *Products obtained in the Perkin reaction.*

	Enol acetate (%)	Diacetate (%)	Residue	Acid (%)
Butanal	41	19	Some	0
2 : 2-Dimethylpropanal	0	0	0	0
3-Methylbutanal	(50)	(not given)	—	—
2-Ethylbutanal	55	25	—	0
Formyl*cyclo*hexane	46	10	Large	0
Heptanal	48 (50)	25 (25)	—	0
Octanal	42 (not given)	23 (not given)	—	0
Acraldehyde	0	32	Large	0
Crotonaldehyde	22	12 *	Large	0
Citral	35	12	Large	0
Cinnamaldehyde	0	0	—	42
Benzaldehyde	0	6	—	50

* Not entirely diacetate.

The Normal Perkin Reaction.—In the present work a number of aldehydes were heated with acetic anhydride or sodium acetate or with both. Heptanal, with acetic anhydride, gave the diacetate (21%) and the enol acetate (20%). Propanal, heated with sodium acetate for a very short time, gave the aldol (50%). The products obtained from various aldehydes with acetic anhydride and sodium acetate together, *i.e.*, under normal Perkin reaction conditions, were as listed in Table 1. Entries in parentheses refer to Semmler's work.[7]

It appears from this Table that saturated aliphatic aldehydes give largely diacetate and enol acetate, with some undefined high-boiling products but no acid. The only exception is the tertiary 2 : 2-dimethylpropanal which cannot form acetates but still gives no acid. Among the unsaturated aldehydes, crotonaldehyde and citral behave similarly. Their enol acetates must be derivatives of butadiene—in the case of crotonaldehyde, 1-acetoxy-1 : 3-butadiene (I). The diacetate fraction contained much dihydro-*o*-tolualdehyde (III) (isolated as its semicarbazone), previously obtained in the reaction of crotonaldehyde with amines.[8] Presumably the acetate (I) reacts in Diels–Alder fashion with the starting aldehyde to give an adduct (II) which loses acetic acid to give the product isolated. Acraldehyde cannot readily give an enol acetate: it did form a diacetate. The formation, together with cinnamic acid, of benzylidene diacetate from benzaldehyde under these conditions does not mean that it is an intermediate,[18] for this diacetate remained unchanged under the conditions of the Perkin reaction. Cinnamaldehyde gives only an acid. From the above it appears that only aromatic aldehydes, and related ones such as cinnamaldehyde, undergo the Perkin reaction. Aliphatic aldehydes either do not react or give acetates and various amounts of high-boiling material of unknown nature.



(I) (II) (III)

The Perkin–Oglialoro Reaction.—In this modification [9] of the Perkin reaction the acid component is phenylacetic anhydride or, more probably, the mixed anhydride of phenylacetic and acetic acid. Reaction with aryl aldehydes takes place very readily because of the activating effect of the phenyl group in stabilising by resonance the reacting

[8] Grundmann, *Chem. Ber.*, 1948, **81**, 513.
[9] Oglialoro, *Gazzetta*, 1878, **8**, 429; 1879, **9**, 428; 1880, **10**, 481.

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anion, $Ph\cdot\bar{C}H\cdot CO_2Ac$. Table 2 shows that no acid was formed from aliphatic saturated aldehydes, but instead considerable amounts of enol acetate and high-boiling substances which were probably diacetate, diphenylacetate, and enol phenylacetate.

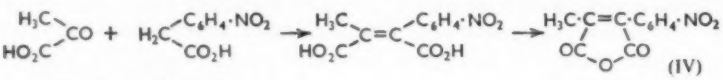
TABLE 2. *Products (%) from aliphatic aldehydes in the Perkin–Oglialoro reaction.*

	Enol acetate	Acid		Enol acetate	Acid
Butanal	31	0	Crotonaldehyde	26	5
2 : 2-Dimethylpropanal	0	0	Citral	30	7
Formyl*cyclo*hexane	24	0	Cinnamaldehyde	0	61
Heptanal	26	Trace			

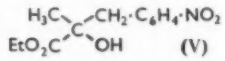
There is a claim [10] to have obtained α-phenylcrotonic acid from paraldehyde. Unsaturated aldehydes gave small yields of acid; cinnamaldehyde gave a high yield of acid. The activation of the acid component, therefore, had enabled the Perkin reaction to take place more readily with aryl and to a slight extent with unsaturated aldehydes, but was not sufficient to bring about reaction with aliphatic aldehydes.

p-*Nitrophenylacetic Anhydride.*—The only successful use of saturated aliphatic aldehydes in the Perkin reaction giving good yields was that recorded by Häffcke and Becker [11] with sodium *p*-nitrophenylacetate and acetic anhydride at 60°. Acetaldehyde gives a good yield of acid, propanal less, 2-methylpropanal much less, and 2 : 2-dimethylpropanal none at all. This was attributed to increasing steric hindrance with the progressive introduction of methyl groups.

In the present work lower temperatures, 35—55°, were generally used. The results are presented in Table 3. Butanal condensed satisfactorily, but higher aldehydes hardly at all. Unsaturated aldehydes reacted well. Even the ketones, pyruvic acid and its ethyl ester, did so too. Other ketones were unreactive, indicating that the lack of reactivity of ketones may well be due to steric hindrance, which is less in pyruvic acid. The carboxyl group is less bulky than an alkyl group and in addition is highly electron-attractive and therefore activating towards the carbonyl group. The product from pyruvic acid appears to be *p*-nitrophenylcitraconic anhydride (IV). Ethyl pyruvate also reacts, but the product is a non-acidic substance $C_{12}H_{15}O_5N$ and hence probably ethyl α-4-nitrobenzyl-lactate (V).



(IV)



(V)

It is clear from the results listed in Table 3 that the further activation by the *p*-nitro-group has improved the reactivity of unsaturated aldehydes and has enabled the lower saturated ones to react. The success of this reagent is undoubtedly due, not only to this activation, but also to the very low temperatures which can be used and which do not lead to diacetate and enol acetate. It proves conclusively that aliphatic aldehydes will undergo the Perkin reaction, if somewhat reluctantly. A study of comparative aldehyde reactivity based on this reaction is reported below. It was mentioned above that benzylidene diacetate was unreactive in the Perkin reaction. The same was found also to apply to acraldehyde diacetate, butanal enol acetate, and crotonaldehyde enol acetate in this reaction. It can therefore be concluded that when acetate formation occurs the Perkin reaction is less likely to succeed.

Higher Aldehydes.—Table 3 shows the non-reactivity of higher aldehydes. In other homologous series loss of reactivity and sudden variation in physical properties have occasionally been observed with increase in chain length, usually in the region of C_5 and C_6,

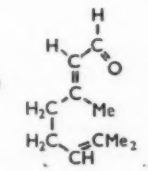
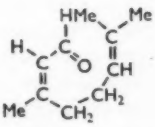
[10] Rupe, *Annalen*, 1909, **369**, 332.
[11] Häffcke and Becker, *J. Org. Chem.*, 1951, **16**, 863.

TABLE 3. *Products from aliphatic aldehydes and* p*-nitrophenylacetic anhydride.*

	This work	Acid (%) and Lit.		This work	Acid (%) and Lit.
Ethanal	—	55 [11]	Ethyl pyruvate	24 (ester)	—
Propanal	—	49 [11]	Acraldehyde	—	38 [a]
Butanal	35	—	Acraldehyde diacetate	0	—
Butanal enol acetate	0	—	Crotonaldehyde	56	40 [b]
2-Methylpropanal	—	12 [11]	Crotonaldehyde enol acetate	0	—
2 : 2-Dimethylpropanal	0	0 [11]	Citral	20	—
Pentanal	1	—	Acetone	0	—
Heptanal	Trace	—	*cyclo*Hexanone	0	—
Pyruvic acid	18	—			

[a] Thielcke and Becker, *J. Org. Chem.*, 1950, **15**, 1241. [b] Gunst, Tobkes, and Becker, *J. Amer. Chem. Soc.*, 1954, **76**, 3595.

e.g., the effect of chain length on the strength of fatty acids.[12] Newman [13] has commented on these variations and has used the term "rule of six" to describe them without attempting a full explanation. The non-reactivity of higher aliphatic aldehydes seems to be a further example of this puzzling rule.

Citral *a*  Citral *b* 

In order to test its applicability the aldehyde, citral, was used. It is known to consist of two isomers, citral *a* (*trans*) and citral *b* (*cis*). In citral *b* the tail of the molecule can coil back against the carbonyl group, whereas in citral *a* it cannot do so unless rotation of the formyl group out of conjugation with the αβ-double bond occurs, which is unlikely because of the loss of resonance energy involved. Citral obtained from lemon-grass oil was treated with acetic anhydride and sodium *p*-nitrophenylacetate, giving the expected acid which was separated, and the remaining citral was recovered. This was subjected once more to the same reaction, but only a trace of acid resulted. On a third treatment no acid was formed. The recovered citral had the expected b. p. and approximate analysis for citral *b*. It gave a semicarbazone of m. p. 170°. The starting citral, which was largely citral *a*, gave a semicarbazone of m. p. 164° (after many crystallisations). These values correspond to those in the literature.[14] It is thus clear that only citral *a* undergoes this Perkin reaction, although it is probably also somewhat hindered. Citral *b* does not react at all because it is more hindered owing to coiling of the chain against the carbonyl group.

Clearly the longer chains of higher aldehydes interfere sterically with the reactivity of the carbonyl group, but no convincing reason has so far been advanced as to how the tail is held in this conformation. Further striking examples of non-reactivity of aldehydes in the Perkin reaction due to increasing chain length will be given (*J.*, 1959, 732).

It is concluded that aliphatic aldehydes fail to undergo the Perkin reaction because of low reactivity and side-reactions. In the higher homologues, from pentanal, there is an additional hindering effect due to chain length.

Attempts to measure comparative carbonyl reactivity have given very contradictory results. For example, Michael [15] claims that aromatic form semicarbazones more readily than do aliphatic aldehydes, but Conant and Bartlett [1] and Westheimer [1] hold the reverse

[12] Bennet and Mosses, *J.*, 1930, 2364; Dippy, *J.*, 1938, 1222.
[13] Newman, *J. Amer. Chem. Soc.*, 1950, **72**, 4783.
[14] Tiemann and Kerschbaum, *Ber.*, 1900, **33**, 877.
[15] Michael, *J. Amer. Chem. Soc.*, 1919, **41**, 393.

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to be true. Stewart [16] found that acetaldehyde gives a bisulphite compound much more quickly than acetone, but Kharasch and Cooper [2] noted that phenylmagnesium bromide reacts much more readily with acetone than with acetaldehyde. The explanation probably is that some of these reactions occur in one stage and others in a sequence of stages. The latter applies to the Perkin reaction.

TABLE 4. *Comparative reactivities of aldehydes in reaction with acetic anhydride and sodium* p-*nitrophenylacetate at* 35°.

Aldehyde	Aromatic	Unsat.	Aldehyde	Aromatic	Unsat.	Aliphatic
o-Nitrobenzaldehyde	13,000	—	Crotonaldehyde	—	130	—
m-Nitrobenzaldehyde	6000	—	*p*-Anisaldehyde	*100*	—	—
p-Nitrobenzaldehyde	6000	—	*p*-*iso*Propylbenzaldehyde	100	—	—
o-Chlorobenzaldehyde	3300	—	*p*-Tolualdehyde	95	—	—
Furfuraldehyde	950	—	*p*-Ethylbenzaldehyde	80	—	—
p-Chlorobenzaldehyde	870	—	Ethanal.....	—	—	69
α-Naphthaldehyde	850	—	α-Methylacraldehyde	—	68	—
Cinnamaldehyde	—	730	Propanal	—	—	27
Benzaldehyde	390	—	Butanal	—	—	15
Acraldehyde	—	280	Heptanal	—	—	0
α-Methylcinnamaldehyde ...	—	140				

Rates for the ordinary Perkin reaction do not appear to have been measured, presumably on account of the high temperatures necessary and the heterogeneous conditions. Measurements have been made with pyridine as a solvent and catalyst,[17] but this is a different type of reaction. As the Perkin–Oglialoro reaction with sodium *p*-nitrophenylacetate takes place at room temperature with both aliphatic and aromatic aldehydes it is well suited for comparisons of reaction rates. Although the reaction mixture is heterogeneous and does not allow of absolute rate measurement, a competitive method in which two aldehydes in considerable excess compete for a limited amount of *p*-nitrophenylacetic anhydride at 35° was found to give sufficiently reproducible results.

When the two aldehydes compete, two acids are formed. These are easily freed from unchanged *p*-nitrophenylacetic acid. Since no side reactions take place at the low temperature used, the composition of the mixture can be determined by titration. Anisaldehyde, which is of intermediate reactivity, was given arbitrarily the value of 100. On this basis comparative reactivities are set out in Table 4. High accuracy is not claimed, but it is not necessary as the reactivities vary over a range of 1000 to 1. It is sufficient to place the aldehydes in order of reactivity.

Among aromatic aldehydes variation in the *para*-substituent has a marked effect, the order being $NO_2 > Cl > H > OMe >$ Alkyl, which is also the order of ability to remove electrons from the carbonyl group. The latter in turn becomes activated for addition. Hence addition to the carbonyl group seems to be the rate-controlling factor.

If this applies in all cases, aliphatic should be more reactive than aromatic aldehydes because in the latter the positive charge on the carbonyl group is spread by the mesomeric effect over the ring system,[3] but from the Table the contrary is manifestly the case. The only other possible rate-determining stage is elimination of water from the intermediate (VI). This would be aided by increasing the negative charge on $C_{(1)}$ and the positive charge on $C_{(2)}$. The nitro-group maintains a positive charge on $C_{(2)}$ in all com-

$$R{\cdot}C_6H_4{\cdot}C_{(1)}H(OH){\cdot}C_{(2)}H(CO_2H){\cdot}C_6H_4{\cdot}NO_2 \quad \text{(VI)}$$

pounds in the series. The negative charge on $C_{(1)}$ would vary with ring substituents R in the order Alkyl $> H > NO_2$, which is the reverse of what is found. Hence elimination is not rate-controlling in aromatic aldehydes, but the slower stage, addition to the carbonyl group, is.

[16] Stewart, *J.*, 1905, **87**, 185.
[17] Buckles and Bremer, *J. Amer. Chem. Soc.*, 1953, **75**, 1487.

Aliphatic aldehydes react very slowly. This is not because the addition stage is slower. Indeed, it ought to be faster. It is because the elimination has become much slower. Elimination is assisted by conjugation in the product or transition state. Such conjugation is present in the cinnamic acids formed from aromatic aldehydes, extending from the ring through the double bond to the carbonyl group. It is present to a smaller extent in the conjugated acrylic acids formed from unsaturated aldehydes and is least in the simple acrylic acids from aliphatic aldehydes: the Table shows the intermediate position of unsaturated aldehydes. It also confirms that the low reactivity of aliphatic aldehydes is due to slow elimination of water.

The inertness of the higher aldehydes, due to coiling, is now confirmed by the low reactivity of butanal and the non-reactivity of heptanal.

Our method provides means of studying electronic and other effects in aromatic aldehydes. The nitro-group and chlorine atom are more effective the *ortho*-position, showing the predominance in both cases of inductive over mesomeric electron-displacement. The high reactivities of cinnamaldehyde and furfuraldehyde are due to decreased steric hindrance in the region of the carbonyl group, for such hindrance is known to affect the Perkin reaction [11] and accounts for the non-reactivity of tertiary aldehydes and most ketones: this is to some extent borne out by the comparatively low reactivity of α-methylcinnamaldehyde.

Experimental

1 : 1-*Diacetoxyheptane and* 1-*Acetoxyhept*-1-*en*-1-*ol.*—Heptanal (20 g.) was refluxed with acetic anhydride (60 ml.) for 8 hr. The product was treated with water and extracted with ether, and this in turn extracted with sodium carbonate solution. No acid was obtained. Distillation of the ether extract gave unchanged aldehyde (4·6 g.), enol acetate (5·1 g.), b. p. 80—90°/10 mm., and diacetate (8·1 g.), b. p. 110—115°/10 mm.

3-*Hydroxy*-2-*methylpentanal.*—Propanal (40 g.) and sodium acetate (11 g.) were heated together on a water-bath for 10 min., poured into water, and extracted with ether and the extract distilled. The fraction of b. p. 85—95°/10 mm. (19·7 g.) was the aldol (semicarbazone, m. p. 198°). Its 2 : 4-dinitrophenylhydrazone, m. p. 154°, did not depress the m. p. of propanal 2 : 4-dinitrophenylhydrazone.

1 : 1-*Diacetoxybutane and* 1-*Acetoxybut*-1-*en*-1-*ol.*—A mixture of butanal (58 g., 1 mol.), sodium acetate (0·5 mol.), and acetic anhydride (1·5 mol.) was refluxed for 8 hr., then poured into water, kept for some time, and extracted with ether. This extract was extracted with sodium carbonate solution, dried, and distilled. The fraction of b. p. 60—75° (10·6 g.) was unchanged aldehyde, that of b. p. 118—120° (37·6 g.) the enol acetate, and that of b. p. 80—82°/6 mm. 1 : 1-*diacetoxybutane* (Found: C, 55·5; H, 8·3. $C_8H_{14}O_4$ requires C, 55·2; H, 8·1%).

The other aldehydes listed in Table 1 were treated in the same fashion. The diacetate from benzaldehyde had m. p. 44·5°; it crystallised after removal of traces of benzaldehyde by means of sodium hydrogen sulphite. Most of the diacetates and enol acetates have already been described. The intermediate " diacetate " fraction from crotonaldehyde consisted largely of dihydro-*o*-tolualdehyde and gave its semicarbazone, m. p. 198° (Found: C, 60·5; H, 7·4; N, 23·2. Calc. for $C_9H_{13}ON_3$: C, 60·3; H, 7·3; N, 23·4%).

Perkin–Oglialoro Reactions (*Table* 2).—The aldehyde (1 mol.), freshly fused sodium phenylacetate (1 mol.), and acetic anhydride (2 mol.) were refluxed together for 5 hr. and poured on ice. The oil was extracted with sodium carbonate solution, to isolate any acid produced. The ethereal extract of the residue was washed, dried, and distilled. The first fraction after removal of ether was unchanged aldehyde, the next enol acetate. Higher fractions were not examined.

From crotonaldehyde there was obtained a small quantity of α-*phenylsorbic acid*, almost colourless needles, m. p. 144° (Found: C, 76·9; H, 6·2. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

From citral a small amount of 5 : 9-*dimethyl*-2-*phenyldeca*-2 : 4 : 8(or 9)-*trienoic acid* resulted, having m. p. 116° (from ethanol) (Found: C, 78·8; H, 8·1. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·2%).

Perkin Reactions using p-*Nitrophenylacetate* (*Table* 3).—The aldehyde (1 mol.), anhydrous sodium *p*-nitrophenylacetate (1 mol.), and acetic anhydride (3 mol.) were heated for 60 hr. at 35° (in some cases 55°) with stirring. A small amount of water was added and stirring continued for 2 hr. The whole was treated with concentrated hydrochloric acid and poured

into water. The ether extract was treated with sodium carbonate solution which on acidification gave the acid product. Any *p*-nitrophenylacetic acid present was removed by boiling water. The acid was recrystallised from aqueous ethanol.

The following acids were analysed: From butanal, 2-p-*nitrophenylhex-2-enoic acid*, m. p. 144°, very pale yellow plates (Found: C, 61·1; H, 5·6; N, 6·2. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·6; N, 6·0%). From crotonaldehyde, α-*p*-nitrophenylsorbic acid, m. p. 229°, pale yellow needles (Found: C, 61·6; H, 5·1. Calc. for $C_{12}H_{11}O_4N$: C, 61·8; H, 4·8%). This acid has been described by Gunst *et al.* (see Table 3). From pyruvic acid, used in the form of its sodium salt, p-*nitrophenylcitraconic anhydride*, yellow prisms, m. p. 124° (Found: C, 57·1; H, 2·7; N, 6·1. $C_{11}H_7O_5N$ requires C, 56·7; H, 3·0; N, 6·0%).

From ethyl pyruvate no acid resulted, but the neutral products afforded *ethyl* α-4-*nitrobenzyllactate* (24%), plates, m. p. 63° (Found: C, 56·8; H, 6·2. $C_{12}H_{15}O_5N$ requires C, 56·9; H, 6·0%).

Citral, b. p. 97°/2 mm., was obtained by vacuum-fractionation of lemon-grass oil. Its semicarbazone melted indefinitely about 130° but after 9 crystallisations at 164°, the value [14] for citral *a*. Citral (20 g.) was treated with sodium *p*-nitrophenylacetate and acetic anhydride in the standard manner but for 80 hr., giving 5 : 9-*dimethyl*-2-p-*nitrophenyldeca*-2 : 4 : 8(or 9)-*trienoic acid*, yellow, m. p. 138° (Found: C, 67·9; H, 6·5; N, 4·0. $C_{18}H_{21}O_4N$ requires C, 68·5; H, 6·7; N, 4·4%). The neutral residue was then washed, dried, and distilled. A fraction (10·4 g.), b. p. 93—98°/2 mm., was citral. This was immediately subjected to reaction again. Acid (1·5%) resulted and a fraction (6 g.), b. p. 98—100°/4 mm., of citral *b* (Found: C, 77·8; H, 10·6. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·6%), which gave a semicarbazone of m. p. 158° rising after two recrystallisations to 170°. On further subjection to the reaction this gave no acid.

Competitive Condensations.—Sodium *p*-nitrophenylacetate (1 mol.), acetic anhydride (5 mol.), and the two competing aldehydes (5 mol. each) were stirred together for 60 hr. at 35°. A stream of dry nitrogen was passed to prevent oxidation. The mixture was then treated with water and either (*a*) the mixture was steam-distilled to remove unused aldehydes and the solid extracted with alkali, or (*b*) the mixture was acidified with mineral acid and extracted with ether and the ether extract shaken with alkali. In all cases the alkaline extract was acidified. The precipitated mixture of acids was washed with boiling water to remove traces of *p*-nitrophenylacetic acid, then redissolved, reprecipitated, filtered off, washed, and dried at 80° for 24 hr. The equivalent weight was then determined by titration with 0·1N-sodium hydroxide. The aldehydes being compared were chosen so that the difference in their molecular weights was as great as possible.

To obtain the results given in the Table the following aldehydes were allowed to compete. Anisaldehyde against acraldehyde (2·81), crotonaldehyde (1·33), acetaldehyde (0·69), propanal (0·265), butanal (0·150), furfuraldehyde (9·46), 2-methylacraldehyde (0·68), and benzaldehyde (3·88); benzaldehyde against cinnamaldehyde (1·87), *p*-tolualdehyde (0·245), *p*-ethylbenzaldehyde (0·197), *p-iso*propylbenzaldehyde (0·264), *o*-nitrobenzaldehyde (33·6), *m*- and *p*-nitrobenzaldehyde (15·57), *o*-chlorobenzaldehyde (8·42), *p*-chlorobenzaldehyde (2·24), α-naphthaldehyde (2·20), and α-methylcinnamaldehyde (0·371). The figures in parentheses represent the ratio of the reactivity of the aldehyde relative to that of anisaldehyde or benzaldehyde. The values for acraldehyde and methylacraldehyde are low because of formation of polymer. Where the ratio is very large or very small excess of the less reactive aldehyde was used.

β-2′-*Furyl*-α-p-*nitrophenylacrylic Acid.*—From the reactions involving furfuraldehyde this *acid* was isolated as yellow needles, m. p. 241° (decomp.) (Found: C, 60·5; H, 3·5; N, 5·2. $C_{13}H_9O_5N$ requires C, 60·2; H, 3·5; N, 5·4%).

α-p-*Nitrophenyl*-4-iso*propylcinnamic Acid.*—This *acid* was isolated from the reactions involving *p-iso*propylbenzaldehyde, as pale yellow prisms (from aqueous alcohol), m. p. 233° (Found: C, 69·2; H, 5·5; N, 4·6. $C_{18}H_{17}O_4N$ requires C, 69·4; H, 5·5; N, 4·5%).

4-*Methyl*-2-p-*nitrophenyl*-2 : 4-*pentadienoic Acid.*—This acid was obtained from reactions involving methylacraldehyde as light brown crystals (from aqueous ethanol), m. p. 164° [cf. Gunst *et al.* (see Table 3)] (Found: C, 61·8; H, 4·9. Calc. for $C_{12}H_{11}O_4N$: C, 61·8; H, 4·8%).

Thanks are accorded to Mr. M. Brachi and to the Uganda Development Corporation for a generous gift of locally produced lemon-grass oil, and to Leverhulme Research Awards Committee for a scholarship (to W. T. L.) with respect to this and the two following papers.

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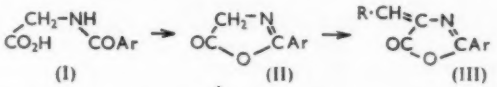
145. *The Erlenmeyer Reaction with Aliphatic Aldehydes, 2-Phenyloxazol-5-one being used instead of Hippuric Acid.*

By MALCOLM CRAWFORD and W. T. LITTLE.

Although aliphatic aldehydes do not readily undergo the Perkin reaction or its modifications the lower members will react readily with 2-phenyl-5-oxazolone and its derivatives in a type of Perkin–Erlenmeyer reaction in which neither acetic anhydride nor sodium acetate with their disturbing side reactions are present. Reaction also takes place readily with aromatic aldehydes and some ketones.

THE Erlenmeyer azlactone synthesis [1] resembles the Perkin reaction. In it an aromatic aldehyde is condensed with hippuric acid in the presence of acetic anhydride and, usually, sodium acetate. It has been suggested [2,3] that hippuric acid (I; Ar = Ph) is first converted into its azlactone, 2-phenyloxazol-5-one (II; Ar = Ph), and that it is this which condenses with the aldehyde (R·CHO) to give the unsaturated azlactone product (III; Ar = Ph).



(I) (II) (III)

It had been assumed [4] that the intermediate (II) was unstable and isolatable only with difficulty but Russian workers [5] have described its convenient preparation in another connection. Obtained thus, in satisfactory yield, it is a yellow crystalline substance of m. p. 86° which is not very stable, presumably partly reverting to hippuric acid and partly undergoing self-condensation. Overheating during the preparation also decomposes it. It must be used within a few hours of preparation.

With aromatic aldehydes it reacts very smoothly, five minutes on the water-bath being sufficient to afford high yields of azlactones. (Sodium acetate is not required; indeed it should be avoided as it causes gum formation probably owing to rapid self-condensation). This ready reaction with aromatic aldehydes confirms the view that it is an intermediate in the Erlenmeyer reaction.

TABLE 1. *Azlactones from aromatic aldehydes and 2-phenyloxazol-5-one.*

	M. p.	Yield [a] (%)	Yield (%) by standard method [a]	Yield (%) claimed
Benzaldehyde	158°	63	58	50—80 [a]
Anisaldehyde	156	55	52	Not given [b] (*ca.* 50)
Furfuraldehyde	171	82	68	70 [c]
Cinnamaldehyde	153	72	61	Not given [d]

[a] Based on equimol. quantities of the reactants. Much higher yields can be obtained by using excess of either.

[a] Gillespie and Snyder, *Org. Synth.*, Coll. Vol. II, 1943, p. 489; Plöchl, *Ber.*, 1883, **16**, 2815. [b] Erlenmeyer and Wittenberg, *Annalen*, 1904, **337**, 294; Dakin, *J. Biol. Chem.*, 1910, **8**, 11. [c] Flatow, *Z. physiol. Chem.*, 1910, **64**, 367. [d] Erlenmeyer and Matter, *Annalen*, 1904, **337**, 271.

In Table 1 the yields obtained by its use from various aromatic aldehydes are compared with those obtained by the standard method with hippuric acid and those previously claimed. This method should prove useful in difficult cases. Aliphatic aldehydes are in fact examples of such difficult cases.

[1] Erlenmeyer, *Annalen*, 1893, **275**, 1.
[2] Baltazzi, *Quart. Rev.*, 1955, **9**, 151.
[3] Havinga and Spitzer, *Rec. Trav. chim.*, 1957, **76**, 173.
[4] Carter, "Organic Reactions," Wiley, New York, 1946, Vol. III, p. 214.
[5] Shemyakin, Lure, and Rodionovskaya, *Zhur. obshchei Khim.*, 1949, **19**, 769; *Chem. Abs.*, 1950, **44**, 1096.

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It was shown in the preceding paper that the failure of aliphatic aldehydes to undergo the Perkin reaction is due partly to low reactivity and partly to acetate formation at high temperatures by the action of acetic anhydride and possibly aldol formation by the action of sodium acetate. Now 2-phenyloxazol-5-one appears to react in Perkin fashion in the absence of both these reagents for it behaves as an anhydride and its methylene group is so reactive that sodium acetate is unnecessary. The fact that it can react at all with aliphatic aldehydes shows that these are not inherently incapable of undergoing this type of reaction but are simply less reactive.

Normally aliphatic aldehydes do not undergo the Erlenmeyer reaction. The expected products have been obtained (though in low yield),[6] especially on use of excess of aldehyde.[7,8] Good yields have been obtained in some cases by the use of lead acetate instead of sodium acetate [9] (see Table 2, method 2). With 2-phenyloxazol-5-one alone, lower aliphatic aldehydes readily give good yields (see Table 2, method 1). The presence

TABLE 2. *Azlactone yields from aliphatic aldehydes and ketones with 2-phenyloxazol-5-one.*

	M. p.	Yield (%), Method 1	Yield (%), with lead acetate, method 2	Previous yield (%)
Ethanal	94°	46	58	20, 39 [7,9]
Propanal	84	38	55	45 [9]
Butanal	56	20	34	7—22 [9]
2-Methylpropanal	87	—	—	31 [9]
2-Ethylbutanal, Heptanal, Octanal	—	0	0	—
Acetone	98—99	—	35	Not given [a]
*cyclo*Hexanone	139—139·5	—	74	49 [b] Very poor

[a] Ramage and Simonsen, *J.*, 1935, 532. [b] Boekelheide and Schramm, *J. Org. Chem.*, 1949, **14**, 298; Billimoria, Cook, and Heilbron, *J.*, 1949, 1437.

of sodium acetate again causes gum formation. Yields are improved by adding lead acetate or even acetic anhydride. Alexander [10] points out the effectiveness of a proton-donor in aiding elimination. Acetic anhydride and lead acetate may act in this capacity, as under the conditions of the reaction they will give small amounts of acetic acid. It is interesting that two of the six ketones tested reacted very well (see Table 2) (ethyl methyl ketone, diethyl ketone, acetophenone, and dipropyl ketone did not give azlactone).

Higher aliphatic aldehydes (above butanal) do not react. This failure was attributed at first to difficulties in isolating the expected azlactones. Their melting points decrease in the normal series with increasing molecular weight. To overcome this, *p*-chloro-, *p*-methyl-, and *p*-phenyl-hippuric acid were prepared. These were readily converted into their phenyloxazolones, which in turn were found also to react smoothly with the lower aliphatic aldehydes. The products from acetaldehyde and benzaldehyde had higher melting points, but none of the three oxazolones reacted with heptanal, which must therefore be considered quite unreactive, doubtless owing to the " coiling " which causes lack of reactivity in the Perkin and the Perkin–Oglialoro reaction (preceding paper).

Some of these substituted hippuric acids and intermediates may be useful in modified Erlenmeyer syntheses on account, not only of higher melting points, but also of higher yields.

[6] Erlenmeyer and Kunlin, *Annalen*, 1901, **316**, 145.
[7] Carter, Handler, and Melville, *J. Biol. Chem.*, 1939, **129**, 359.
[8] Corse, Kleiderer, and Soper, *J. Amer. Chem. Soc.*, 1948, **70**, 438.
[9] Finar and Libman, *J.*, 1949, 2726.
[10] Alexander, " Principles of Ionic Organic Reactions," Wiley, New York, 1950, pp. 181—183; see also Noyce and Snyder, *J. Amer. Chem. Soc.*, 1958, **80**, 4324.

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Experimental

2-Phenyloxazol-5-one.—Hippuric acid (20 g.) and acetic anhydride (130 ml.) were heated on a water-bath for 20 min. with frequent shaking, then poured into benzene (200 ml.) and ice-water (200 ml.) and stirred for 30 min. The benzene layer was stirred with 1% sodium hydrogen carbonate solution (2 l.) until all acetic anhydride had been removed, washed, and dried, and the benzene was removed below 40°. The resulting solid on recrystallisation from benzene gave yellow plates (10 g.), m. p. 86°.

Reactions of 2-Phenyloxazol-5-one.—Aromatic aldehydes. The aldehyde (1 mol.) and 2-phenyloxazol-5-one (1 mol.) were heated together on the water-bath for 5 min., then poured on ice. The crystals which separated were filtered off, washed with 70% ethanol and recrystallised from ethanol. Yields and m. p.s are in Table 1.

Aliphatic aldehydes and ketones. Method 1. As the method for aromatic aldehydes gave only gums, lower temperatures and longer times were used. Propanal (1 mol.) and 2-phenyloxazol-5-one (1 mol.) were heated together at 50° for 3 hr. The yellow crystals obtained by pouring the mixture on ice were extracted with ether, and the extract filtered and evaporated in the presence of an equal volume of water. The pale yellow needles, m. p. 83° (38%), were recrystallised from 50% ethanol.

Method 2. Propanal (1 mol.), 2-phenyloxazol-5-one, and lead acetate (0·3 mol.) were treated together for 10 min. on the water-bath. The solid obtained on pouring the mixture on ice was washed with aqueous ethanol and recrystallised from ethanol (m. p. 84°; 55%).

Method 3. Propanal was treated as in method 2, but with acetic anhydride (3 mol.) in place of lead acetate, giving material (44%), m. p. 84°. The results by methods 1 and 2 are given in Table 2. The acetaldehyde runs were carried out in sealed bottles for longer times at room temperature.

Azlactones from 2-p-Tolyloxazol-5-one.—p-Toluoylglycine (5 g.), m. p. 161°, was converted into 2-*p*-tolyloxazol-5-one (3·2 g.) (as above), yellow plates, m. p. 101—101·5° (from benzene–ligroin). With benzaldehyde it gave *4-benzylidene-2-p-tolyloxazol-5-one* (56%), greenish-yellow plates (from benzene–ethanol), m. p. 184·5° (Found: C, 77·8; H, 4·9; N, 5·4. $C_{17}H_{13}O_2N$ requires C, 77·6; H, 5·0; N, 5·3%). With acetaldehyde there was obtained by method 2 but in 8 hr. at 25° a 48% yield of *4-ethylidene-2-p-tolyloxazol-5-one*, almost colourless needles, m. p. 124—124·5° (Found: C, 71·4; H, 4·9; N, 6·9. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5; N, 7·0%).

p-Chlorobenzoylglycine (5 g.), m. p. 143°, was converted into 2-*p*-chlorophenyloxazol-5-one (2·8 g.), pale yellow needles (from ligroin), m. p. 121—122°. With benzaldehyde it gave *4-benzylidene-2-p-chlorophenyloxazol-5-one* (80%), yellow needles (from benzene–ethanol), m. p. 179° (Found: C, 67·6; H, 3·7; N, 4·9. $C_{16}H_{10}O_2NCl$ requires C, 67·7; H, 3·6; N, 4·9%). This compound (1 g.) was refluxed with 8% sodium hydroxide solution (10 ml.) until all dissolved. On cooling, filtration, and acidification of the filtrate a white solid separated which on crystallisation from aqueous ethanol gave *α-p-chlorobenzamidocinnamic acid*, needles, m. p. 238° (Found: C, 63·7; H, 4·2; N, 4·4. $C_{16}H_{12}O_3NCl$ requires C, 63·7; H, 4·0; N, 4·6%). With acetaldehyde there was obtained by method 2, but for 20 hr. at 25°, *2-p-chlorophenyl-4-ethylideneoxazol-5-one* (65%), needles (from ethanol), m. p. 158° (Found: C, 59·4; H, 3·8; N, 5·9. $C_{11}H_8O_2NCl$ requires C, 59·6; H, 3·6; N, 6·2%).

p-Phenylbenzoylglycine.—p-Phenylbenzoyl chloride, m. p. 113° (6 g.), was added gradually to glycine (5 g.) and 10% sodium hydroxide solution (50 ml.) with shaking. On acidification a solid was precipitated which on recrystallising (with charcoal) from ethanol gave the *acid* as plates, m. p. 211° (decomp.) (4·2 g.) (Found: C, 70·9; H, 5·3. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1%).

This acid (5 g.) was converted into 2-diphenylyloxazol-5-one (2·4 g.), yellow plates (from ligroin), m. p. 143° (decomp.). With benzaldehyde it gave *4-benzylidene-2-diphenylyloxazol-5-one* (64%), yellow needles (from benzene–ethanol), m. p. 191·5—192° (Found: C, 81·8; H, 4·3; N, 4·1. $C_{22}H_{15}O_2N$ requires C, 81·2; H, 4·6; N, 4·3%). With acetaldehyde there was obtained by method 2, but for 20 hr. at 25°, 2-diphenylyl-4-ethylideneoxazol-5-one (64%), pale yellow plates (from benzene–ethanol), m. p. 122°.

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146. *The Inhibiting Effect of Chain-lengthening on Aldehyde Reactivity in the Perkin Reaction.*

By MALCOLM CRAWFORD and W. T. LITTLE.

The lower aliphatic ethers of *o*-, *m*-, and *p*-hydroxybenzaldehyde undergo the Perkin reaction readily. As the chain-length of the alkyl group increases the yield of substituted cinnamic acid at first remains constant, then decreases abruptly at the point at which the end of the chain can reach the carbonyl group. This exemplifies the " rule of six."

NEWMAN [1] formulated a " rule of six " to correlate the abrupt change in reactions and properties which occurs in many carbonyl compounds with increase in chain length. The sixth atom from the carbonyl-oxygen interacts in an unspecified fashion with the carbonyl group owing to chain-coiling. Examples in ascending homologous series are the sudden increase in strength at butyric acid,[2,3] variation in esterification and hydrolysis rates of fatty acids and their esters,[4] changes in optical rotation,[5] and movement of reaction sites in aliphatic ketones.[6] The Perkin reaction of lower aliphatic aldehydes with sodium *p*-nitrophenylacetate and acetic anhydride [7] succeeds only with lower members: [8] the inertness of the higher homologues is a further example of the rule of six. Coiling is also responsible for the inertness of citral *b*, but reactivity of citral *a*. Inertness was also found in the reaction of 2-phenyloxazol-5-one with higher aldehydes.[8] Some examples of failure of aromatic aldehydes to give the Perkin reaction are reported below.

The double bond in citral stiffens the molecule. Other molecules can be more effectively stiffened by the introduction of a benzene ring, whose *ortho*-, *meta*-, and *para*-positions can be used to secure different rigid lengths. Various alkoxybenzaldehydes have been subjected to the normal Perkin reaction, results being given in the table together with others already known.

	Yield (%) of the cinnamic acid from RO·C_6H_4·CHO		
R	*ortho*	*meta*	*para*
Me	44 [a]	39 [a]	30 [c]
			20 [a]
Et	43	Reacts readily [b]	36 [d]
Pr[n]	3·2	12	40 [d]
Bu[n]	0·22	7·6	35
			40 [d]

	Yield (%) of the cinnamic acid from RO·C_6H_4·CHO		
R	*ortho*	*meta*	*para*
C_5H_{11}	0·16	2·1	0·1
C_6H_{13}	—	0	Trace
$C_{10}H_{23}$	—	—	Trace [d]
5-Nitro-2-pentyloxy	16	—	—

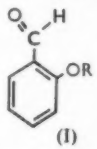
[a] Lock and Bayer, *Ber.*, 1939, **72**, 1064. [b] Werner, *Ber.*, 1895, **28**, 1997. [c] Posner, *J. prakt. Chem.*, 1910, **82**, 425. [d] Stoermer and Wodarg, *Ber.*, 1928, **61**, 2323.

In the *meta*-series the yield decreases with chain-length to zero at R = C_6H_{13}. The *m*-propoxy-compound is the first to be affected. In it the side-chain does not quite reach to the van der Waals touching distance from the carbonyl group, as indicated by Catalin models. *m*-Propoxybenzaldehyde may be compared to *n*-butyraldehyde which is the shortest aliphatic aldehyde to show a decrease in yield in a Perkin–Oglialoro reaction.[8] It has a " six number " [1] of 3. Newman's notation cannot, however, be used in partly rigid molecules, but the effect is the same, namely, a reduction in reactivity when the end of the chain can approach the reactive group.

[1] Newman, " Steric Effects in Organic Chemistry," Wiley, New York, 1956, p. 206.
[2] Dippy, *J.*, 1938, 1222.
[3] Bennett and Mosses, *J.*, 1930, 2364.
[4] Newman, *J. Amer. Chem. Soc.*, 1950, **72**, 4783.
[5] Smith and McReynolds, *ibid.*, 1939, **61**, 1963.
[6] Alexander, " Principles of Ionic Organic Reactions," Wiley, New York, 1950, p. 128.
[7] Häffcke and Becker, *J. Org. Chem.*, 1951, **16**, 863.
[8] Crawford and Little, preceding papers.

In the *para*-series Stoermer and Wodarg [9] observed without comment that, whereas the lower members up to butoxy react readily to give the cinnamic acids, *p*-cetyloxybenzaldehyde gives a negligible yield. Repetition with the inclusion of some intermediate members confirms this. *p*-Pentyloxybenzaldehyde is found to be the lowest member in which a decrease of yield occurs. *p*-Hexyloxybenzaldehyde gives only a trace of product. Hence in the *para*-series the decrease in yield takes place at a higher point than in the *meta*-series, showing that the effect is not due to some inherent property of a particular chain length. It begins at that chain-length (C_5) which is almost long enough to impinge on the carbonyl group if the chain follows the shortest path that its valency angles will allow. The formyl group is assumed to remain always coplanar with the ring. In *p*-hexyloxybenzaldehyde, which is practically non-reactive, the side chain can readily reach the formyl group. The fall in yield is much sharper in this series.

In the *ortho*-series, as might be expected, complications arise. In *o*-methoxybenzaldehyde the methyl group is already in close proximity to the formyl group yet reaction takes place readily, as also with the *o*-ethoxy-compound. It is with *o*-propoxybenzaldehyde that falling off first takes place. This becomes reasonable if one assumes that in *o*-substituted benzaldehydes the formyl group occupies the reversed planar position (I) (or, much less likely, a non-planar position) owing to steric repulsion by the *ortho*-substituent. The carbonyl group can then be reached readily by an *o*-butoxy-group, almost by an *o*-propoxy-group, but not by an *o*-ethoxy-group. Yields are in keeping with this.



(I)

In all three series yields fall off appreciably as soon as the chain is long enough to reach almost to the van der Waals radius of the carbonyl oxygen atom. It is difficult to see how the chain is held in this position, especially at the temperature of the reaction (~160°) since the force holding it there is not strong enough even to twist the formyl group in *o*-ethoxybenzaldehyde out of the plane of the ring. For fatty acids Dippy [2] suggested a hydrogen bond O · · · H but this would be extremely weak. It is more likely that the side chain interferes sterically with an intermediate state such as a transition complex or the hydroxy-intermediate. There is no evidence whether the side-chain interferes with the stability or with the reactivity of the intermediate.

o-Pentyloxybenzaldehyde gives only a 0·16% yield in the Perkin reaction. Its 5-nitro-derivative gives a 16% yield which, however, is much less than that from *m*-nitrobenzaldehyde; thus reactivity is restored by activation.[8]

In Dippy's curve [2] illustrating the strengths of fatty acids, in addition to the marked increase between propionic and butyric acid, there is a sharp fall between octanoic and nonanoic acid which he did not explain (see also ref. 5). A scale model shows that in nonanoic acid the chain can continue past the C=O group until the end methyl group reaches the carboxylic hydroxyl group, a result which might perhaps affect the acid strength.

Experimental

Preparation of Aldehydes.—The hydroxybenzaldehyde (1 mol.), alkyl bromide (2 mol.), and potassium hydroxide (0·4 mol.) were refluxed in ethanol or, for higher alkyl bromides, *cyclo*hexanone, for 24 hr. The cold product, in ether, was extracted with potassium hydroxide solution. The ether layer, when washed, dried, and distilled under reduced pressure, gave the aldehyde. Apart from the following, which are new, the aldehydes had b. p.s in agreement with those given in the literature: *o*-Pentyloxybenzaldehyde, b. p. 167°/15 mm. [*semicarbazone*, needles (from aqueous alcohol), m. p. 178° (Found: C, 62·7; H, 7·5; N, 16·8. $C_{12}H_{19}O_2N_3$ requires C, 62·6; H, 7·7; N, 16·9%)]; with fuming nitric acid at <10° it gave *5-nitro-2-pentyloxybenzaldehyde*, yellow plates (from aqueous alcohol), m. p. 44° (Found: C, 60·7; H, 6·1; N, 6·1. $C_{12}H_{15}O_4N$ requires C, 60·8; H, 6·4; N, 5·9%) [*semicarbazone*, yellow needles, m. p. 221° (Found: C, 53·8; H, 6·1. $C_{13}H_{18}O_4N_4$ requires C, 53·1; H, 6·2%)]. *m*-Pentyloxybenzaldehyde, b. p. 156°/10 mm. [*semicarbazone*, needles (from aqueous alcohol), m. p. 166° (Found: C, 63·6; H, 8·0; N, 16·4. $C_{13}H_{19}O_2N_3$ requires C, 62·6; H, 7·7; N, 16·9%)].

[9] Stoermer and Wodarg, *Ber.*, 1928, **61**, 2323.

Perkin Reaction.—The aldehyde (1 mol.), acetic anhydride (2 mol.), and sodium acetate (0·6 mol.) were heated at 160—180° for 8 hr. The acid formed was isolated in the usual way, recrystallised from aqueous acetic acid, dried, and weighed. Yields are given in the Table. Among them the following are new: o-*Butoxy*-, needles, m. p. 96° (Found: C, 71·0; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%), o-*pentyloxy*-, needles, m. p. 85° (Found: C, 71·9; H, 7·7. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%), 5-*nitro*-2-*pentyloxy*-, needles, m. p. 145° (Found: C, 61·0; H, 6·1; N, 5·0. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1; N, 5·0%), m-*propoxy*-, plates, m. p. 135·5° (Found: C, 69·0; H, 6·2. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%), m-*butoxy*-, needles, m. p. 91·5° (Found: C, 70·7; H, 7·4%), and m-*pentyloxy-cinnamic acid*, plates, m. p. 75° (Found: C, 71·4; H, 7·7%).

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147. *Electrical Conductances of Solutions in Nitric Acid. Part III.* Solutions of Dinitrogen Tetroxide.*

By J. D. S. GOULDEN, W. H. LEE, and D. J. MILLEN.

Electrical conductances and transport numbers are reported for solutions of dinitrogen tetroxide in nitric acid. The electrical conductances are comparable with those of alkali-metal nitrates in nitric acid. The transport measurements are interpreted in terms of the cathode process $NO_2^+ + e \longrightarrow NO_2$ and the reverse process at the anode. It is concluded that dinitrogen tetroxide is almost completely ionised in dilute solutions in nitric acid.

THREE modes of ionisation of dinitrogen tetroxide in dilute solution are known: in water NO_2^- and NO_3^- are produced, in strong acids such as sulphuric acid NO^+ and NO_2^+ are formed, and under other conditions the intermediate ionisation leads to NO^+ and NO_3^-. The present study extends previous Raman [1] and infrared spectroscopic studies [2] of the last type of ionisation in nitric acid as solvent, by investigating the electrical conductance and transport properties of these solutions.

EXPERIMENTAL

Materials.—Nitric acid was prepared as described in Part I.[3] Dinitrogen tetroxide was prepared by dropping fuming nitric acid on potassium nitrite, passing the gases through phosphoric oxide tubes, and condensing the product in a trap cooled in alcohol–solid carbon dioxide. The condensate was purified by re-distillation in a stream of oxygen and condensed as a white solid at −80°. Solutions were prepared by distillation into the acid in a current of oxygen.

Electrical Measurements.—Conductances were determined at −10° as described in Part I, and are recorded in Table 1. In the transport-number determinations solutions were electrolysed in a Hittorf apparatus modified as illustrated in Fig. 1 to prevent the loss, by subsequent migration, of NO_2^+ formed in the anode compartment. In order to avoid contamination of the solution the taps for isolating the compartments were left unlubricated but sealed with solution. The phosphoric oxide tubes and the stoppers covering the taps prevented the entry of water vapour during electrolysis. Depending on the solution concentration, $1—5 \times 10^{-3}$ F, as measured by a copper coulometer in series, was passed through the cell, the quantity of electricity being corrected for inaccuracies inherent in this type of coulometer (Part II). After electrolysis the contents of the compartments were analysed for stoicheiometric NO_2 as described in Part II.

* Part II, *J.*, 1958, 2248.

[1] Goulden and Millen, *J.*, 1950, 2620.
[2] Millen and Watson, *J.*, 1957, 1369.
[3] Lee and Millen, *J.*, 1956, 4463.

The migration of the nitrosonium ion together with the cathode process $NO_2^+ + e \longrightarrow NO_2$, which was discussed in Part II, results in a net gain of $(1 + 2t_{NO^+})$ moles of stoicheiometric NO_2 per Faraday. Transport numbers calculated on this basis are listed in Table 2. Evaluation of transport numbers from the change in the anode compartment on the basis of the reverse electrode reaction $NO_2 \longrightarrow NO_2^+ + e$ gave slightly lower values. This difference

FIG. 1. *Transport apparatus.*

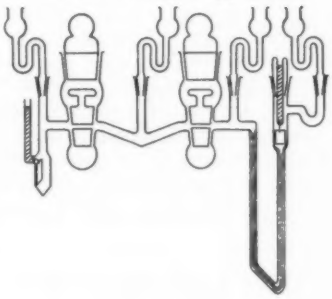
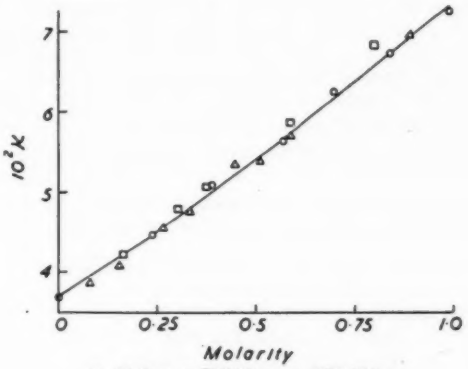


FIG. 2. *Comparison of conductances of dinitrogen tetroxide and of ammonium and potassium nitrates.*



○, N_2O_4; △, KNO_3; □, NH_4NO_3.

almost certainly arises from a slight intervention of the anode reaction $NO_3^- \longrightarrow NO_2^+ + \frac{1}{2}O_2 + 2e$, the usual anode process in the electrolysis of solutions of nitrates in nitric acid as established in Part II. The contribution of this process becomes more pronounced as the concentration of dinitrogen tetroxide decreases.

TABLE 1. *Specific conductances and densities of solutions of dinitrogen tetroxide in nitric acid.* $T = -10{\cdot}02°$.

N_2O_4(M)	0·0699	0·2400	0·3874	0·5694	0·6970	0·8422	0·9725	1·208	1·869
$10^4\kappa$ (ohm^{-1})	365·0	446·3	509·1	565·5	626·1	674·6	730·2	812·2	996·0
d_4^{-10}	1·5645	1·5685	1·5715	1·5752	1·5785	1·5819	1·5849	1·5911	

TABLE 2. *Transport numbers of the nitrosonium ion in solutions of dinitrogen tetroxide in nitric acid.*

$T = -10°$.	N_2O_4 (M)	0·1442	0·2793	0·3728	0·4136	0·5152	0·5808	0·7016	1·577
	t_{NO^+}	0·047	0·077	0·115	0·131	0·176	0·160	0·237	0·377
	l_{NO^+}	13·1	12·7	15·3	16·2	19·0	16·0	21·2	—
$T = 20°$.	N_2O_4 (M)	0·0497	0·110	0·181	0·379	0·420	0·831	1·242	1·535
	t_{NO^+}	0·053	0·093	0·138	0·193	0·197	0·282	0·302	0·326

DISCUSSION

Fig. 2 shows that the specific conductance of a solution of dinitrogen tetroxide is entirely comparable with that of potassium or ammonium nitrates in nitric acid over the whole range of concentration investigated. If it is accepted that alkali-metal nitrates are completely ionised in these solutions, it is difficult to avoid the conclusion that dinitrogen tetroxide must be very largely ionised. The high conductance cannot arise from a large ionic mobility of the nitrosonium ion, for the data in Table 2 show that over most of the concentration range the transport numbers of the nitrosonium ion are slightly smaller than those given in Part II for the alkali-metal ions in nitric acid solution. The transport numbers of Table 2 are not as accurate as those of the alkali-metal ions, particularly for the dilute solutions. Here they are small because of the large contribution to the conductance by the ions formed by solvent self-dissociation, and so are sensitive to errors

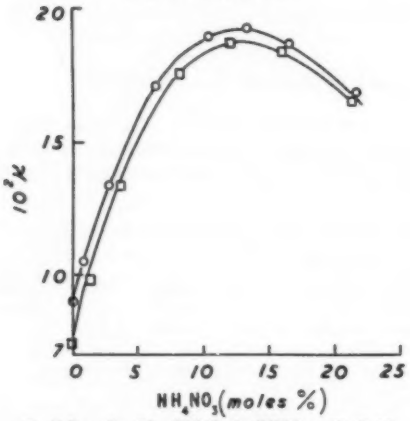
arising from unavoidable small losses of the tetroxide by vaporisation during electrolysis. Although the mobilities of the ions show some scatter, and increase with increasing concentration, the values are all within the range 17 ± 4 ohm^{-1}, showing that the mobility of the nitrosonium ion cannot be significantly greater than the mobilities of sodium, potassium, or ammonium ions. Thus the results are well understood in terms of the nearly complete ionisation $N_2O_4 \longrightarrow NO^+ + NO_3^-$. They could scarcely be accounted for by any type of ionisation which provides less than one nitrate ion per molecule of dinitrogen tetroxide. The possibility of an incomplete ionisation which provides more than one nitrate ion per dinitrogen tetroxide molecule, *e.g.*,

$$N_2O_4 \rightleftharpoons 2NO_2; \quad NO_2 + HNO_3 \longrightarrow HNO_2^+ + NO_3^-$$

is excluded by the observed magnetic susceptibilities of the solutions.[2]

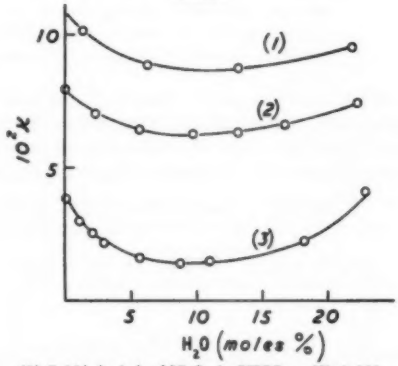
The sensitivity of the ionisation $N_2O_4 \rightleftharpoons NO^+ + NO_3^-$ to repression by added nitrate ion provides in principle a method for determining the strength of dinitrogen tetroxide as an electrolyte in these solutions. Some evidence in this direction may be obtained from the conductivity study by Taylor *et al.*,[4] whose results can be used to find the increment in conductance produced by a given amount of the tetroxide in solutions containing varying quantities of ammonium nitrate. If the tetroxide were a strong

FIG. 3. *Effect on conductances of adding ammonium nitrate.*



○, 3·2 moles % of N_2O_4 in HNO_3; □, 3·48 moles % of N_2O_5 in HNO_3.

FIG. 4. *Effect on conductances of adding water.*



(1) 5·4% (w/w) of N_2O_4 in HNO_3; (2) 4·4% (w/w) of N_2O_4 in HNO_3; (3) HNO_3 solvent.

electrolyte, the increment would be expected to be independent of the amount of added nitrate ion, within the limits of the approximation of concentration-independent ionic mobilities. The increment varies little over the range 0—6 moles % of added nitrate ion for an approximately 0·85M-solution of dinitrogen tetroxide.

We may compare the effect of adding ammonium nitrate to solutions of similar concentrations of dinitrogen tetroxide and pentoxide. The curves of Fig. 3 apply to solutions of these oxides in nitric acid, initially at 3·2 and 3·48 moles %, respectively. These concentrations will change as ammonium nitrate is added to the system, and it is not possible, in the absence of density data for the resulting solutions, to calculate concentrations after each addition of ammonium nitrate; the variation is not expected to be large, however. The decrease in κ with increasing concentration of ammonium nitrate, observed at the higher concentrations, is almost certainly a viscosity effect, such as has been previously found in very concentrated solutions;[5] the important point is that the

[4] Taylor, Baker, and Lyne, *Canad. J. Chem.*, 1951, **29**, 452.
[5] Berl and Saenger, *Monatsh.*, 1929, **54**, 1036.

two curves run closely parallel. It is unlikely that nitronium nitrate is incompletely ionised in these solutions, and so there is no evidence from conductivity measurements of any marked repression of the ionisation of dinitrogen tetroxide, in 3 moles % solution, by up to six-fold increase in nitrate-ion concentration.

The effect of addition of water on the conductances of solutions of the tetroxide in nitric acid may also be calculated from the data of Taylor *et al.*[6] Fig. 4 shows that the increase in conductance produced by a given amount of tetroxide is approximately independent of the amount of water present in the solvent, up to about 20 moles % of water, indicating that dinitrogen tetroxide is largely ionised in these aqueous nitric acid solutions. The same limitations as mentioned previously apply to the calculation of the concentrations. The rather slower initial decrease in conductance on addition of water to the solutions, as compared with the pure acid, probably arises because of the partial repression of the solvent ionisation due to the nitrate ion produced by the tetroxide already added. For solvents containing more than about 20 moles % of water the increment in conductance due to added tetroxide falls off, but the rapidly increasing concentration of $H_3O^+NO_3^-$ makes interpretation difficult in this region.

Although the evidence indicates that the dinitrogen tetroxide is a strong electrolyte in nitric acid solution, it is clear from the yellow colour of these solutions that ionisation cannot be complete. The solutions have an absorption with a molar extinction coefficient, calculated on the basis of stoicheiometric tetroxide, of the order of 10 at 4400 Å, and of the order of 100 at 4000 Å. The absorption was followed into the ultraviolet region but no maximum could be observed. This is attributed to the overlap of bands due to NO_2 and possibly N_2O_4, with maxima at approximately 4000 Å and 3400 Å respectively as observed in the gas phase,[7] with a band centred at about 3000 Å due to the nitrate ion,[8] followed by the absorption of the solvent itself. Since there is no absorption maximum, the measurements cannot be used to determine the concentration of undissociated NO_2, for quantitative estimates obtained from values on the rising side of an absorption band are subject to large uncertainties by a shift in the position of the absorption band in passing from the gas to solution.

A comparison of relative intensities at a number of wavelengths on the side of the absorption band has been made for various concentrations. Typical results of optical-density ratios obtained for successive dilutions of an approximately 0·8M-solution are given below. The optical densities of these solutions were measured at room temperature by a Unicam spectrophotometer, glass-stoppered cells being used. Readings were taken for each solution at a number of wavelengths, since the sensitivity at any given wavelength varies with the concentration.

Dilution factor	1	2	3	4	Dilution factor	1	2	3	4
λ (Å)	Ratio of optical densities				λ (Å)	Ratio of optical densities			
4700	1	0·546	0·306	0·200	5000	1	0·582	0·345	0·235
4800	1	0·552	0·325	0·225	5100	1	0·650	0·345	0·232
4900	1	0·562	0·354	0·214					

The volatility of dinitrogen tetroxide is a complicating factor in these experiments, but within the accuracy of measurements made on the side of an absorption band, it appears that Beer's law is obeyed, supporting previous work[9] on this system. This indicates that the concentration of NO_2 is directly proportional to the stoicheiometric concentration over this range. This is the result to be expected for the operation of the equilibria:

$$2NO_2 \rightleftharpoons N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

[6] Taylor, Lyne, and Follows, *Canad. J. Chem.*, 1951, **29**, 439.
[7] Hall and Blacet, *J. Chem. Physics*, 1952, **20**, 1745.
[8] Morton and Riding, *Proc. Roy. Soc.*, 1926, *A*, **113**, 717.
[9] Lynn, Mason, and Corcoran, *J. Phys. Chem.*, 1955, **59**, 238.

if the concentration of the species N_2O_4 is small. The concentration of the species NO_2 has already been shown to be small by magnetic-susceptibility measurements.[2]

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148. *Some Aspects of the Anion-exchange Behaviour of Uranyl Nitrate in the Presence of Other Inorganic Nitrates.*

By J. K. Foreman, I. R. McGowan, and T. D. Smith.

The addition of inorganic nitrates to aqueous solutions of uranyl nitrate enhances the uptake of uranium on the anion-exchange resin Deacidite FF in the order aluminium > calcium > lithium > ammonium. The predominating cause is considered to be the facilitation of formation of nitrate complexes by the uranyl ion, and of the subsequent ion-exchange, due to the decrease in the effective water content of the system resulting from hydration of the added cation. Visible absorption spectra revealed no new peaks ascribable to an anionic uranyl nitrate complex.

Kraus and his co-workers [1] have shown that the anion-exchange behaviour of certain metal ions in hydrochloric acid is markedly influenced by the presence of inorganic chlorides. Similarly the profound effect of aluminium nitrate on the uptake of uranyl uranium on the anion-exchange resin Deacidite FF from aqueous solutions of uranyl

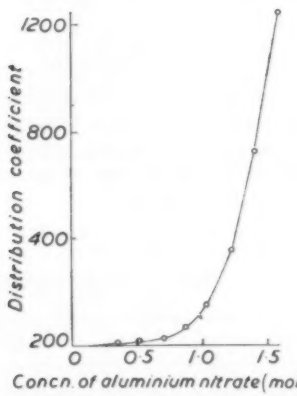


Fig. 1. *Variation of distribution coefficient of uranium with aluminium nitrate concentration.*

nitrate has recently been noted.[2] This study has now been extended to calcium, lithium, and ammonium nitrate, and attempts have been made to correlate the results with changes in visible absorption spectra which occur on the addition of other nitrates to solutions of uranyl nitrate.

Fig. 1 illustrates the size of the increase in the distribution coefficient K_d of uranium (ratio of the equilibrium concentration of uranium in the resin phase to that in the aqueous

[1] Nelson and Kraus, *J. Amer. Chem. Soc.*, 1954, **76**, 5916; Kraus, Nelson, Clough, and Carlston, *ibid.*, 1955, **77**, 1391; Kraus, Moore, and Nelson, *ibid.*, 1956, **78**, 2692.
[2] Ockenden and Foreman, *Analyst*, 1957, **82**, 592.

XUM

phase) on Deacidite FF when increasing amounts of aluminium nitrate are added to aqueous uranyl nitrate. Fig. 2 compares the extents to which aluminium, calcium, lithium, and ammonium nitrates influence the exchange at constant nitrate-ion concentration (6M) maintained by nitric acid. The addition of hydrogen ion, as perchloric or

FIG. 2. *Variation of distribution coefficient of uranium with concentration of* Al, Ca, Li, *and* NH_4 *ions. Nitrate-ion concentration constant at* 6M.

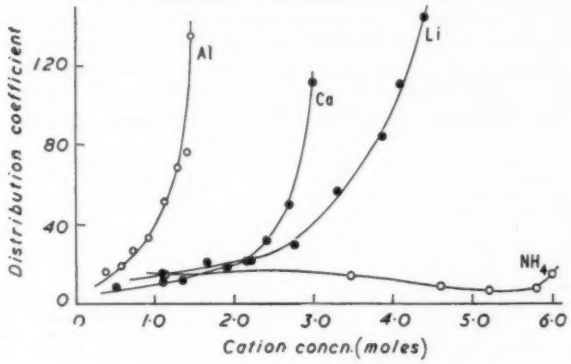


FIG. 3. *Variation of distribution coefficient of uranium with perchloric acid concentration. Aluminium nitrate concentration constant at* 1·3M.

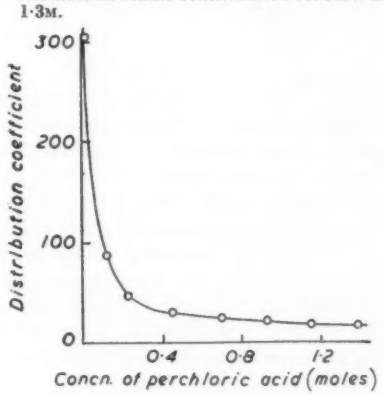
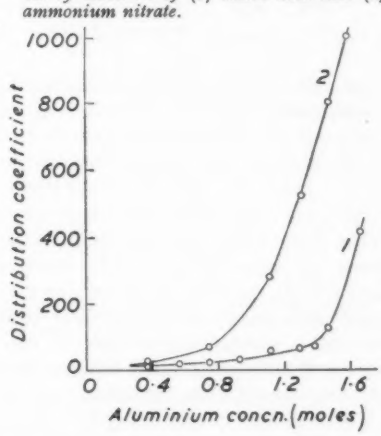


FIG. 4. *Variation of distribution coefficient of uranium with aluminium-ion concentration. Nitrate-ion concentration kept at* 6M *by addition of* (1) *nitric acid and* (2) *ammonium nitrate.*



nitric acid, to a fixed concentration of uranyl and aluminium nitrates decreases the uranium uptake (Figs. 3 and 4, curve 1), and addition of ammonium ion (Fig. 4, curve 2) has little influence (cf. Fig. 2).

The greatly enhanced anion-exchange of uranium caused by aluminium, calcium, or lithium nitrate in weakly acid solutions must be attributed to the formation of an anionic nitrate complex of uranium. Formulation of this complex as $UO_2(NO_3)_3^-$, rather than a species of higher negative charge, is supported by the work of Betts and Michels [3] who found that nitrate complex-formation of the uranyl ion is comparatively weak $\{K = [UO_2(NO_3)^+]/[UO_2^{2+}][NO_3^-] = 0{\cdot}21 \pm 0{\cdot}01$ at 5·38M-ionic strength$\}$. Further, from

[3] Betts and Michels, *J.*, 1949, 286.

spectrophotometric data they found no conclusive evidence for the existence of a higher nitrate complex in nitric acid–sodium nitrate mixtures of ionic strength up to 7·05M. The observed decrease in extent of exchange on addition of nitric acid (Fig. 4, curve 1) may then be reasonably explained as due to formation of the uncharged, associated species $HUO_2(NO_3)_3$ in equilibrium with $UO_2(NO_3)_2$ and nitric acid.

The extent to which uranium is taken up on the resin will depend on the extent of formation of $UO_2(NO_3)_3^-$ and the exchange mechanism by which it is adsorbed. Both these processes will be governed to an appreciable extent by the free water content of the system. In the presence of a high concentration of aluminium nitrate much of this water will be preferentially bound to the aluminium ions, and the formation of the complex uranyl nitrate anion, which involves replacement of water from the hydration sphere of the uranyl ion will be enhanced. Similarly the anion-exchange reaction, which proceeds

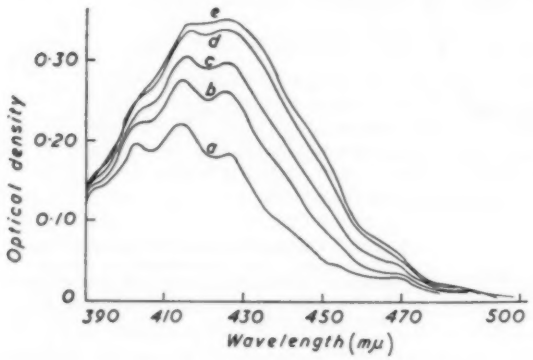


FIG. 5. *Absorption spectra of* 0·005M-*uranyl nitrate*: (*a*) *in water*; (*b*) *in* 0·7M-, (*c*) *in* 1·02M-, (*d*) *in* 1·39M-, *and* (*e*) *in* 1·57 -*aluminium nitrate.*

through removal of water from the hydrated anionic species, will also be facilitated. Since the progressive addition of aluminium nitrate enhances both these effects simultaneously the shape of the distribution coefficient curve can be understood. The smaller abilities of calcium, lithium, and ammonium nitrate to promote anion-exchange of uranium should therefore follow the order of tendency of these cations to be hydrated. If partial molal entropies are taken as a measure of this tendency the values are [4] −74·9, −13·2, 3·4, and 26·9 cal. deg.$^{-1}$ mole^{-1} for the ions Al^{3+}, Ca^{2+}, Li^+, and NH_4^+, the order being that expected. Indeed, the ammonium ion, the least effective in promoting formation of the anionic uranyl nitrate complex, is known to distort the water structure the least of the cations studied, and produces the smallest change in the entropy of water.[5] Hindman [6] has advanced a similar explanation to correlate the relative effectiveness of mixtures of ammonium nitrate and nitric acid, calcium nitrate and nitric acid, and nitric acid alone, in promoting complex-ion formation.

A second factor increasing the anion-exchange of the uranyl nitrate complex is the variation in activity coefficients of the species present, both in solution and in the resin phase. Such variations are likely to be considerable in the concentrated salt solutions used, but the lack of quantitative data, particularly for resin-phase activities, precludes detailed discussion.

Measurements of the absorption spectrum of uranyl nitrate in the presence of varying quantities of aluminium nitrate indicate that no significant change accompanies the marked increase in distribution coefficient in the region of M-aluminium nitrate, which therefore

[4] Latimer, "Oxidation Potentials," Prentice Hall, New York, 1952.
[5] Frank and Robinson, *J. Chem. Phys.*, 1940, **8**, 933; Fajans and Johnson, *J. Amer. Chem. Soc.*, 1942, **64**, 668.
[6] Hindman, Paper 45 in "The Transuranium Elements" (Ed. Seaborg, Katz, and Manning), McGraw-Hill, New York, 1949.

cannot readily be associated with higher anionic nitrate complexes, and supports the view that only one anionic complex is formed by the dehydration effect postulated above. Fig. 5 shows that increasing the concentration of aluminium nitrate intensifies the spectral absorption uniformly over the wavelength range 400—470 mμ and no new absorption peaks are revealed. This contrasts with the well-known effect on the spectrum of uranyl nitrate on adding increasing amounts of nitric acid (Fig. 6) where additional absorption peaks occur at 436, 451, and 467 mμ, the intensities of which increase with increasing nitric acid concentration.

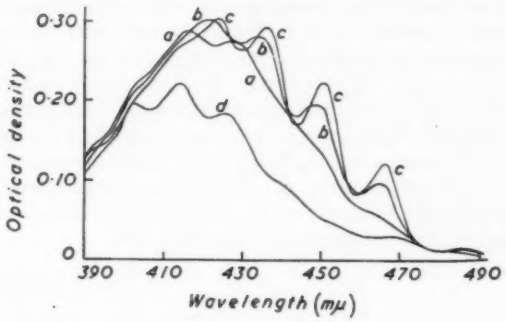


FIG. 6. *Absorption spectra of* 0·005M-*uranyl-nitrate*: (*a*) *in* 4·05M-, (*b*) *in* 9·30M-, *and* (*c*) *in* 13·90M-*nitric acid*; (*d*) *in water.*

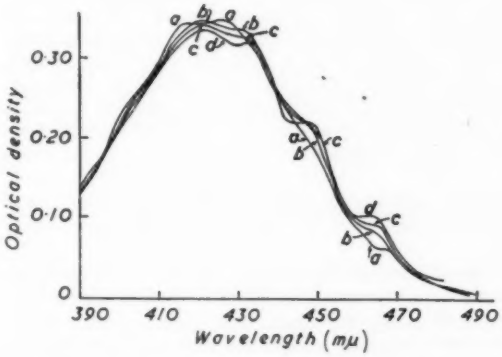


FIG. 7. *Absorption spectra of* 0·005M-*uranyl nitrate in* 1·22M-*aluminium nitrate and constant nitrate concentration of* 6·76M *maintained by ammonium nitrate.* [HNO_3] = (*a*) 0, (*b*) 1·5M, (*c*) 2·33M, (*d*) 3·1M.

Since solutions of uranyl nitrate in nitric acid show very little anion-exchange (see Table), it may be supposed, in agreement with Kaplan *et al.*,[7] that curve *C* of Fig. 6 is due

Anion-exchange distribution coefficients for uranyl nitrate in nitric acid.

Resin: Deacidite FF. Vol. of solution/weight of resin = 100 : 1.

Acidity (M)	5	6	7	8	9	10
K_d	1	4	11	15	8	3

to the presence of an appreciable concentration of the associated species $HUO_2(NO_3)_3$. From their studies on the absorption spectrum of uranyl nitrate in organic solvents in the presence of quaternary ammonium nitrates, where the new peaks noted above are still further intensified, Kaplan *et al.*[7] consider that the singly charged anion $UO_2(NO_3)_3^-$ also exhibits a spectrum of the type shown in Fig. 6, curve *C*. This is apparently at variance with the present work, as Fig. 7 shows. The decreasing anion-exchange observed on the addition of increasing amounts of nitric acid to a solution of uranyl nitrate in aluminium nitrate is paralleled by the increasing growth of the (initially absent) peaks at 436, 451, and 467 mμ, supporting the assignment of the spectrum of Fig. 6, curve *C*, to

[7] Kaplan, Hildebrandt, and Ader, U.S.A.E.C. Report ANL 4520.

$HUO_2(NO_3)_3$. However, no firm conclusion can be drawn from this discrepancy since the present spectra refer to aqueous solutions whereas those of Kaplan *et al.* were derived from solutions in organic solvents and some variation in spectrum from solvent to solvent was observed.

Lower nitrate complexes such as $UO_2(NO_3)^+$ and $UO_2(NO_3)_2$ also contribute to the spectra shown in Figs. 5, 6, and 7. Thus an appreciable spread in values resulted in attempting to calculate the formation constant for $HUO_2(NO_3)_3$ according to $UO_2(NO_3)_3^- + H^+ \rightleftharpoons HUO_2(NO_3)_3$ by the method of Betts and Michels [5] using the data of Fig. 7 (constant $[NO_3^-]$, varying $[H^+]$) at uranium concentrations of 5×10^{-3}M and 1×10^{-2}M, and assuming curve *C*, Fig. 6, to represent the spectrum of $HUO_2(NO_3)_3$. Also optical densities of identical nitrate mixtures but varying uranium concentration do not obey Beer's law. The presence of lower nitrate complexes is consistent with the low values observed [3,8] for the stepwise formation constants of nitrate complexes of the uranyl ion. The spectrophotometric evidence shows that even in strong solutions of aluminium nitrate the formation of $UO_2(NO_3)_3^-$ is far from complete, and the rapid increase in anion-exchange uptake of uranium in aluminium nitrate concentrations of greater than M must be attributed primarily to the facilitation of anion-exchange resulting from hydration of the added aluminium ion as discussed above.

Experimental

Values of distribution coefficients were obtained from batch equilibration experiments in which solutions of the required concentrations were made up, having a constant total volume of 20 ml. and containing constant total amounts of uranyl nitrate (1·040 mg. of U per ml.) and resin (0·200 g.). The mixtures were allowed to equilibrate for 3 days with alternate standing and mechanical shaking. Commercial Deacidite FF was dried at 40°, then ground mechanically, and the particles of 60—85 mesh retained and washed with 3N-sodium hydroxide and then distilled water, the fines being removed by this process. It was converted into the nitrate form by contact with 2N-nitric acid. After filtration and washing with a little water, the resin was allowed to dry in air.

The thiocyanate spectrophotometric method [9] was used to determine the uranium content of solutions, and the absorbancy of the solutions was measured in 2 cm. cells by a Hilger Spekker spectrophotometer with Ilford H.556 filters.

Spectral data were obtained by using a Hilger Uvispek spectrophotometer at 390—500 mμ at 2 or 3 mμ intervals, 4 cm. glass cells being used throughout. The constant uranyl nitrate concentrations employed for this work were 0·005M and 0·010M.

The standard uranyl nitrate solution for anion-exchange studies was prepared by dissolving the requisite amount of pure uranyl nitrate in water. A spectroscopically pure specimen was employed for the spectral investigations. Aluminium nitrate solution was prepared from reagent-grade material, and aluminium analysed as the oxinate. Data for calcium and lithium nitrate solutions were obtained from solubility tables,[10] and perchloric acid by titration with standard alkali. Constancy of total nitrate concentration was achieved by ammonium nitrate addition except where otherwise stated.

Thanks are offered to F. Barker for the experimental results quoted in the Table, and to the Managing Director, United Kingdom Atomic Energy Authority (Industrial Group), for permission to publish this paper.

Chemical Services Department, U.K.A.E.A.(I.G.), Windscale Works,
Seascale, Cumberland.
Chemistry Department, Royal College of Science and Technology,
Glasgow, C.1. [*Received, August 18th*, 1958.]

[8] Ahrland, *Acta Chem. Scand.*, 1951, **5**, 1271.
[9] Currah and Beamish, *Analyt. Chem.*, 1947, **19**, 609.
[10] Seidell, "Solubilities of Inorganic and Metal Organic Compounds," Van Nostrand, New York, 1940.

149. *The Mechanism of Oxidation of α-Glycols by Periodic Acid. Part V.** cyclo*Hexane*-1 : 2-*diols.*

By G. J. Buist, C. A. Bunton, and J. H. Miles.

The kinetic form of the periodate oxidation of *cis*- and *trans-cyclo*hexane-1 : 2-diol shows that an intermediate complex is formed. The equilibrium constant is greater for the *trans*-isomer, but the rate constant of breakdown of the *cis*-complex is much the larger. The values of equilibrium and rate constants are compared with those of the butane-2 : 3-diols.

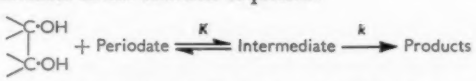
The first kinetic study of the periodate oxidation of the *cyclo*hexane-1 : 2-diols showed that, at 25°, and with pH <8 in water, the rate decreased with increasing pH. The rate of oxidation of the *cis*-diol was *ca.* 30 times that of the *trans*-diol, and it was suggested that this was because the hydroxyl groups of the *cis*- but not the *trans*-diol were in convenient positions for formation of a cyclic intermediate with the periodic acid.[1]

Our aim was to relate the periodate oxidations of the *cyclo*hexane-1 : 2-diols to those of other 1 : 2-diols, and to obtain evidence for formation of intermediate complexes between diols and periodate. We found that, as for other diols, addition of either diol to an aqueous solution of periodate, at 0°, gave an immediate decrease in pH. This suggests that intermediates are formed rapidly, and decompose slowly to the reaction products, and that they are stronger acids than periodic acid.[2]

Kinetics.—The methods were those used in earlier work.[2] With diol in large excess over periodate a plot of the reciprocal of k' (the first-order rate constant with respect to periodate) against the reciprocal of the diol concentration [G] was a straight line, with a positive intercept. This is the kinetic form observed first for the oxidation of ethanediol,[3] and subsequently for the oxidations of a number of 1 : 2-diols.[4,5] It is usually expressed as:

$$1/k' = 1/kK[\mathrm{G}] + 1/k \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k and K are constants in the reaction sequence:



(Periodate represents the totality of periodic acid and its ions.)

Observation of this kinetic form (eqn. 1) does not, of itself, prove that the reactants and intermediate complex are in equilibrium, nor does it necessarily give true values of k and K [although the value of k so determined is approximately correct (Part IV)]. As a test for equilibrium we compared the slopes of the " reciprocal plots " (eqn. 1) with the reciprocals of the limiting second-order constants, k_s. If the reactant concentrations are reduced sufficiently the concentration of the intermediate complex tends to zero and the kinetic order to second. In the limit when both [G] and [Periodate] $\longrightarrow 0$, $k_s = kK$ if the system is in equilibrium.[5] Then the equilibrium constant $K = k_f/k_b$ (k_f and k_b are the rate constants for the reversible reaction between diol and periodate to form the intermediate complex [6]). Reactants and the intermediate are in equilibrium when the rate of decomposition back to reactants is much greater than its rate of decomposition to products, *i.e.*, when $k_b \gg k$.

Our kinetic results are summarised in the Experimental section, where we list values of

* Part IV, *J.*, 1957, 4580.

[1] Price and Knell, *J. Amer. Chem. Soc.*, 1942, **64**, 552.
[2] Buist and Bunton, *J.*, 1954, 1406.
[3] Duke, *J. Amer. Chem. Soc.*, 1947, **69**, 3054.
[4] Duke and Bulgrin, *ibid.*, 1954, **76**, 3903.
[5] Buist, Bunton, and Miles, *J.*, 1957, 4567.
[6] *Idem, ibid.*, 1957, 4574.

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"k" and "K," the apparent rate and equilibrium constants respectively, as determined from the "reciprocal plots." From comparisons between the values of k_s and "kK" we conclude that the reactants and the intermediate complex of the *cis*-diol are in equilibrium at pH > 7. This test could not be applied to the *trans*-diol, because the equilibrium constant is too high in alkaline solution (cf. Part IV). However, we assume that, as for other diols, reactants and intermediate complex are in equilibrium in alkaline solution.

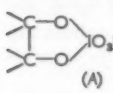
From these rate and equilibrium constants we can calculate the rate constant k_1 for breakdown of the single negatively charged intermediate complex (cf. ref. 2). The value of the equilibrium constant K at pH 9 is that of the equilibrium constant K'' between the periodate dianion, $H_3IO_6^{2-}$, the diol, and the dinegatively charged intermediate complex. This is because the dissociation constants are such that both periodate and intermediate exist largely as dianions in solutions of pH 9.[2,5]

Discussion.—The chair form of *cyclo*hexane is energetically preferred to the boat form.[7] The *cis*-diol in the chair form can have its hydroxyl groups in the axial-equatorial conformations, but the *trans*-diol can have these groups in either the axial-axial or the equatorial-equatorial conformation. The *trans*-diol exists preferentially in the equatorial-equatorial conformation both in water [8] and in non-hydroxylic solvents; [9] the energy barrier for interconversion is probably not large (cf. the interconversion of the conformations of *trans*-1 : 2-dichloro*cyclo*hexane [10]). The calculated inter-oxygen distance is *ca.* 2·86 Å for both the *cis*-diol and the *trans*-diol in the equatorial-equatorial conformation.[11] It is close to the value of 2·73 Å for the distance [12] between adjacent oxygen atoms in the ion $H_3IO_6^{2-}$. Thus the hydroxyl-oxygen atoms of both the *cis*- and the *trans-cyclo*hexanediol

Left: *Intermediate complex of the* trans-*diol* (*equatorial-equatorial conformation*); *bonds joining oxygen atoms "a" to iodine are in the plane of the paper.*
Right: *Intermediate complex of the* cis-*diol*; *bonds joining oxygen atoms "a," "a'" to iodine are out of the plane of the paper, "a'" being away from the observor.*
In both models, two of the oxygen atoms joined to iodine are omitted. ◎ *Iodine.* ○ *Oxygen.* ● *Carbon.*

should be able to co-ordinate with the octahedral iodine atom to form a strain-free puckered ring [5] with only slight changes in their original interatomic distances. The situation is therefore different from that for the formation of cyclic ketals,[11] where the ring formed will be nearly planar, as it probably will be for borate complexes. In these cases ring formation occurs most readily with the *cis*-diol.

The arguments do not necessarily apply to the formation of neutral or mononegatively charged periodate complexes. These may exist in a dehydrated form with a penta-co-ordinated iodine atom,[2] *e.g.*, (*A*). Such a dehydrated complex could have a structure more akin to that of a borate complex. There is slight experimental evidence for this because the apparent value of K in acid solution is greater for the *cis*- than for the *trans*-diol, in contrast to their relative values at higher pH. However, we must also consider steric repulsions between atoms in the octahedral intermediate complexes. Suggested structures of the dinegatively



(*A*)

[7] Hassell, *Quart. Rev.*, 1953, **7**, 221.
[8] Whiffen, *Chem. and Ind.*, 1956, 964.
[9] Kuhn, *J. Amer. Chem. Soc.*, 1952, **74**, 2492; 1954, **76**, 4323.
[10] Tulinskie, Giacomo, and Smyth, *ibid.*, 1953, **75**, 3552.
[11] Angyal and Macdonald, *J.*, 1952, 686.
[12] Helmholtz, *J. Amer. Chem. Soc.*, 1937, **59**, 2036.

charged forms of the intermediate complex are shown in the Figure (this representation is similar to that used earlier for the structures of intermediate complexes from periodate and open-chain diols[5]). There are no large internal repulsions in the dinegatively charged intermediate complex from the *trans-cyclo*hexanediol, but there is interference between one of the oxygen atoms attached to the iodine atom and one of the carbon atoms (marked *b*), or the hydrogen atoms attached to it, in the dinegatively charged intermediate complex of the *cis*-diol. Distortion of the *cyclo*hexane ring into a flattened half-chair structure would reduce this interference, but it would introduce further strains in both the *cyclo*hexane and the periodate ring of the complex, and the actual geometry of the complex will depend upon the relative importance of these internal strains.

We can now compare the structures of the intermediate complexes of the *cyclo*hexane-1 : 2-diols with those of the butane-2 : 3-diols.[5] The intermediate complex of the *meso*-butane-2 : 3-diol has one methyl group in a "hindered" position, with interference between this group and one of the oxygen atoms of the periodate. The structure of this complex is therefore similar to that of the *cis-cyclo*hexane-1 : 2-diol, and the equilibrium constant K'' for formation of the dinegatively charged complex is very similar for both these diols (Table 1). Thus the favourable orientation of the hydroxyl groups of *cis-cyclo*hexane-1 : 2-diol, which should facilitate complex formation, is outweighed by internal repulsions in the complex. These repulsions may be less severe for the complex of the open-chain *meso*-butane-2 : 3-diol than for the more rigid fused-ring system of the complex from *cis-cyclo*hexane-1 : 2-diol.

TABLE 1. *Rate and equilibrium constants.*

Diol	10^4k_1 (sec.$^{-1}$)	K'' (mole^{-1} l.)	$10^3K'_1$ (mole l.$^{-1}$)	$10^7K'_2$ (mole l.$^{-1}$)
*cis-cyclo*Hexane	3300	400	0·83	0·48
trans- „	165	1000	3·11	0·85
(−)-Butane-2 : 3-	308	8000	3·4	0·42
meso- „	182	373	2·6	0·50

The structure of the dinegatively charged intermediate complex of *trans-cyclo*hexane-1 : 2-diol is similar to that of (−)-butane-2 : 3-diol, and there is no large interference between the atoms of the *cyclo*hexane ring and the oxygen atoms of the periodate (see Figure). The equilibrium constant K'' is less for *trans-cyclo*hexane-1 : 2-diol than for (−)-butane-2 : 3-diol. This may be due to disruption of some intramolecular hydrogen-bonding[9] during complex formation, or to the distortion of the *cyclo*hexane ring which must occur when the distance between the hydroxyl-oxygen atoms is reduced (by *ca.* 0·1 Å) in forming the octahedral complex. (The latter effect will be much smaller than for formation of a cyclic ketal where, because of formation of a nearly planar ring, the reduction of the inter-hydroxyl distance will be *ca.* 0·5 Å.[11])

Thus we have the situation that, in this particular case, the equilibrium constant for complex formation at high pH is greater for the *trans-* than for the *cis*-diol (Table 1). This comes about because of the arrangement of oxygen atoms around the octahedral iodine atom in the dinegatively charged intermediate complex. It may not occur in the neutral or mononegatively charged intermediate complexes, because these may exist in dehydrated forms with only five oxygen atoms around the iodine atom. We are not able to test this point, because meaningful equilibrium constants can be determined only for the dinegatively charged complexes. However, the "apparent" equilibrium constants (from the "reciprocal plots") in acid solution are greater for the *cis-cyclo*hexane-1 : 2-diol, a reversal of the situation in alkaline solution (see Experimental section). Because the neutral and the mononegatively charged complexes may exist in either hydrated or dehydrated forms comparisons between their equilibrium constants might be misleading, even if we could measure them.

There is no evidence, from this work, that the greater stability of the *trans-* than

of the *cis*-complex (relative to the reactants) will extend to more rigid ring systems, or to co-ordinating agents other than periodate.

We have calculated ionisation constants for the complexes. They are given with those for the intermediate complexes of the butane-2 : 3-diols [5] in Table 1. The values, except for that of the first ionisation constant K'_1, of the complex of *cis-cyclo*hexane-1 : 2-diol, are little affected by changes in structure or configuration.

The rate of breakdown, to products, of the mononegatively charged complex of *cis-cyclo*hexane-1 : 2-diol is ~20 times that for the *trans*-complex. This factor is much larger than that between the complexes of the butane-2 : 3-diols.[5]

TABLE 2. *Second-order rate constants for oxidation of the* cyclo*hexane*-1 : 2-*diols at* 0°; [reactants] *ca.* 10^{-3}M.

pH	0·98	4·30	7·30	8·80	9·86
cis-	0·42	2·8	6·9	1·1 *	0·98 *
trans-	0·033	0·58	0·41	0·007 *	—

* These values are kK from the slopes of the " reciprocal plots."

The high reactivity of the mononegatively charged complex of the *cis*-diol may be caused by internal steric strains, which are released by breakdown, but it is possible that the proportion of the mononegatively charged intermediate which exists as a reactive dehydrated form [2] may be greater for the *cis*- than for the *trans*-diol.

These results show that the faster oxidation of the *cis*- than of the *trans*-diol is due, not to ease of intermediate-complex formation, but to the rapid breakdown of this complex. The rate of reactions with glycol-splitting reagents is sometimes used for determination of configuration. However, it is often difficult to interpret the kinetic effects of structural changes for multi-stage reactions, and this is particularly so for periodate oxidations because here the rate has a complicated dependence upon equilibrium and rate constants. The generalisation that a *threo*-isomer is more reactive towards periodate than an *erythro*-isomer seems to be well-founded experimentally [3,4,5] and is supported by what we know of the detailed mechanism, but the generalisation that a *cis-cyclo*hexanediol is more reactive than the *trans*-diol is much less reliable as a structural test. Exceptions to it are well known,[14] and it is therefore desirable to consider the details of the reaction mechanism, and the non-bonding interactions which may occur in any intermediate complexes of the reaction wherever such a test is applied.

EXPERIMENTAL

Materials.—The diols were prepared from *cyclo*hexene which had been purified by treatment with sodium hydrogen sulphite and fractionated under nitrogen; it had b. p. 82°, n_D^{25} 1·444.

The *trans*-diol was prepared *via* the chlorohydrin and recrystallised from ethyl acetate; it had m. p. 101—103°.[15]

The *cis*-diol was prepared by oxidation of *cyclo*hexene with *tert.*-butyl hydroperoxide, catalysed by osmium tetroxide. It was recrystallised from ethyl acetate and had m. p. 97—99°.[16]

Kinetics.—Addition of one drop of a 6M-solution of the *trans*-diol in water to 0·1M-periodate at pH 7·07 gave an immediate fall in pH of 0·32 unit. A similar experiment with the *cis*-diol gave a pH change from 9·03 to 8·92.

Runs, at 0°, were followed with diol in excess, or with reagents in comparable, low concentrations. The iodometric methods were those described earlier.[2]

Because it may be of interest to compare the rates of oxidation in regions for which we did not observe formation of an intermediate complex in equilibrium with reactants, we report rate constants for all the kinetic runs.

[13] Zuman, Sicher, Krupicka, and Svoboda, *Nature*, 1956, **178**, 1407.
[14] Levesley, Waters, and Wright, *J.*, 1956, 840; Criegee, Hoger, Huber, Kruch, Marktscheffel, and Schellenberger, *Annalen*, 1956, **599**, 81.
[15] Coleman and Johnson, *Org. Synth.*, Coll. Vol. I, p. 151.
[16] Milas and Sussman, *J. Amer. Chem. Soc.*, 1937, **59**, 2347.

Rate constants have the units of sec.$^{-1}$ for first-order and sec.$^{-1}$ mole^{-1} l. for second-order reactions. Concentrations are those at the beginning of a run. The value of k at pH 4 was taken as k_1 (cf. ref. 2), and K'_1 and K'_2 (the first and second ionisation constants of the intermediate complex) were calculated by the use of equations (11*a*) and (10*b*) of ref. 2. The value of the equilibrium constant K in alkaline solution is taken as K''. The values of k give reliable values of the rate constant for breakdown of the complex even when the system is not in equilibrium (cf. Part IV).

cis-*Diol*. Results were:

pH 0·98, ionic strength 0·130 mole l.$^{-1}$.

10^2[diol] (M)	0·980	1·265	1·83	2·04	3·49	9·10
$10^3k'$	7·68	11·5	13·6	16·0	17·9	33·2

The reciprocal plot gives $10^2k = 3·3$, and $K = 40$ mole^{-1} l. The limiting second-order rate constant $k_s = 0·42$ (from runs with 10^3[diol] = 2·64M, and 10^3[periodate] = 0·731M, having $k_2 = 0·423$, and 10^4[diol] = 1·56M, and 10^3[periodate] = 0·700M, having $k_2 = 0·417$). The value of k_s does not agree with that of kK (from the reciprocal plot), so equilibrium conditions do not hold.

pH 4·30, ionic strength 0·021 mole l.$^{-1}$.

10^2[diol] (M)	0·850	1·15	1·30	1·56	2·53	3·53
$10^3k'$	3·95	5·37	5·18	6·72	8·86	13·0

$k = 0·33$, and $K = 15$ mole^{-1} l.

$k_s \gtrsim 2·8$ (from runs with 10^3[diol] = 1·60M, and 10^3[periodate] = 0·64M, having $k_2 = 3·2$, and 10^3[diol] = 1·26M, and 10^3[periodate] = 0·62M, having $k_2 = 2·4$). Equilibrium conditions do not hold.

pH 7·30, ionic strength 0·123 mole l.$^{-1}$.

10^2[diol] (M)	0·850	1·12	1·37	2·15	3·34	8·44
$10^2k'$	4·09	4·95	5·76	6·99	7·53	8·49

$k = 0·11$ and $K = 72$ mole^{-1} l.

$k_s \gtrsim 7$ (from runs with 10^3[diol] = 2·61M, and 10^3[periodate] = 0·648M, having $k_2 = 6·22$, and 10^3[diol] = 1·03M, and 10^3[periodate] = 0·678M, having $k_2 = 7·67$). The value of k_s agrees with the value of 8·0 for kK, and we conclude that reactants and complex are in equilibrium. We assume, by analogy with oxidation of other diols, that equilibrium will be maintained at higher pH.

pH 8·80, ionic strength 0·100 mole l.$^{-1}$.

10^2[diol] (M)	0·730	0·972	1·817	3·04	9·38
$10^3k'$	2·00	2·19	2·36	2·36	2·71

From calculation by the method of least squares we estimate $10^3k = 2·7$, and $K = 410$ mole^{-1} l.

pH 9·86, ionic strength 0·120 mole l.$^{-1}$.

10^2[diol] (M)	1·11	1·74	2·51	9·31
$10^4k'$	2·37	2·56	2·68	2·92

$10^4k = 3·0$, and $K \sim 330$ mole^{-1} l.

trans-*Diol*. Results were:

pH 0·98, ionic strength 0·130 mole l.$^{-1}$.

10^2[diol] (M)	0·637	1·161	3·11	7·78
$10^3k'$	0·474	0·769	1·60	2·66

$10^3k = 4·76$, and $K = 16·8$ mole^{-1} l.

$k_s = 3·3$ (from runs with 10^3[diol] = 1·94M, and 10^3[periodate] = 1·07M, having $10^2k_2 = 3·22$, and 10^3[diol] = 2·02M, and 10^3[periodate] = 0·679M, having $10^2k_2 = 3·46$). Equilibrium conditions do not hold.

pH 4·30, ionic strength 0·021 mole l.$^{-1}$.

10^2[diol] (M)	1·03	1·32	1·85	2·39	3·33	9·07	9·48
$10^3k'$	0·745	0·909	1·04	1·07	1·18	1·46	1·41

$10^3k = 1·65$, and $K = 83$ mole^{-1} l.

$k_s = 0{\cdot}58$ (from runs with with 10^3[diol] = 1·44M, and 10^3[periodate] = 0·739M, having $k_2 = 0{\cdot}59$, and 10^3[diol] = 2·11M, and 10^3[periodate] = 0·736M, having $k_2 = 0{\cdot}56$). Equilibrium conditions do not hold.

pH 7·30, ionic strength 0·124 mole l.$^{-1}$.

10^3[diol] (M)	0·947	1·16	1·70	3·88	9·43
$10^3k'$	2·56	2·71	2·76	2·88	3·03

$10^3k = 3{\cdot}06$, $K \approx 580$ mole^{-1} l.

Because of the high value of the equilibrium constant we could not reach sufficiently low reactant concentrations for observation of a limiting second-order rate constant, k_2.

pH 8·80, ionic strength 0·100 mole l.$^{-1}$.

10^3[diol] (M)	0·554	1·01	1·57	9·96
$10^3k'$	6·40	6·44	6·86	7·06

$10^3k = 7{\cdot}2$, $K \approx 1000$ mole^{-1} l.

We assume that this value of K gives a reliable value for K'', because we know from observations on the open-chain diols [2,6] that reactants and intermediate complex are in equilibrium at pH 9.

William Ramsay and Ralph Forster Laboratories,
University College, Gower Street, London, W.C.1. [*Received, September 4th*, 1958.]

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150. *Vapour Pressures of Metal Alkoxides. Part II.*[1] *Zirconium Tetra*-tert.*-butoxide and -amyloxide.*

By D. C. Bradley and J. D. Swanwick.

The vapour pressures of zirconium tetra-*tert.*-butoxide and -amyloxide have been measured by the static method in the pressure ranges 0·06—162 mm. Hg and 0·02—42 mm. Hg respectively. The results were confirmed by hypsometric measurements in the pressure ranges 9·5—464 mm. Hg and 2·5—42 mm. Hg respectively. The data show that the zirconium compounds are more volatile than the corresponding titanium compounds over the regions studied.

Recently [1] we reported measurements of the vapour pressures of titanium *tert.*-butoxide and -amyloxide made in a specially designed apparatus. Now we report measurements on zirconium tetra-*tert.*-butoxide and -amyloxide in the same type of apparatus. In addition the current results have been checked and confirmed with an all-glass hypsometer.

Experimental

Preparation of Zirconium Tetra-tert.*-alkoxides.*—Both compounds were prepared by alcohol interchange involving purified zirconium *iso*propoxide solvate and the appropriate tertiary alcohol. For the *tert.*-amyloxide the method used was essentially that already described [2] whilst for the *tert.*-butoxide a large excess of *tert.*-butyl alcohol–benzene azeotrope (*ca.* 3·5 l.) was added to the *iso*propoxide (*ca.* 40 g.) and the *iso*propyl alcohol–benzene azeotrope was fractionated out during 2 weeks' continuous distillation through an efficient column (130 cm., packed with Fenske glass helices). In each case the *tert.*-alkoxide was vacuum-distilled and analysed before being finally purified for vapour-pressure measurements. The zirconium contained 0·5% of hafnium but, in view of the small difference in volatilities of zirconium and hafnium *tert.*-alkoxides, no correction was applied to the vapour pressures.

Vapour-pressure Measurements.—(i) *The static method.* Most of the work was carried out by this method which was described in full previously.[1] The same criteria of purity were also employed.

(ii) *Hypsometer method.* Whilst the static method has proved invaluable for measurements on these extremely reactive compounds its major virtue, the detection of decomposition, has

[1] Part I, Bradley and Swanwick, *J.*, 1958, 3207.
[2] Bradley, Mehrotra, and Wardlaw, *J.*, 1952, 4204.

also been a limitation in that it has set an upper limit to the temperature at which reliable measurements could be made. Moreover, the volatilities of zirconium and hafnium *tert.*-alkoxides are so close that it was desirable to check the static results by an independent method. A hypsometric method was chosen because it was considered to be least affected by the products of decomposition and could thus be used at higher temperatures. The all-glass hypsometer and adaptor shown in Fig. 1 fitted on to the vacuum-purification line of the static apparatus at the BS14 joint 3. The sample (10—15 c.c.) of alkoxide, purified as in the static measurements, was caused by the dropper 1 to fall cleanly through the key of the high-vacuum tap 2 into the hypsometer. After closure of tap 2 the hypsometer unit was transferred to the manometer side of the static apparatus, and pure dry nitrogen was admitted. The hypsometer was immersed to a depth which just covered the boiler 4 in a thermostat-controlled bath. Smooth ebullition was promoted by carefully purified glass wool in vessel 4. The thermometer pocket 8 was placed well above the boiler to avoid superheating by radiation and the wide-diameter tubes 6 and 7 facilitated conduction of the vapour stream past point 8—this is very important at the lower pressures. The condenser pocket 9 was well away from pocket 8 and

FIG. 1. *Boiling-point apparatus and adaptors. (Outside diameters shown.)*

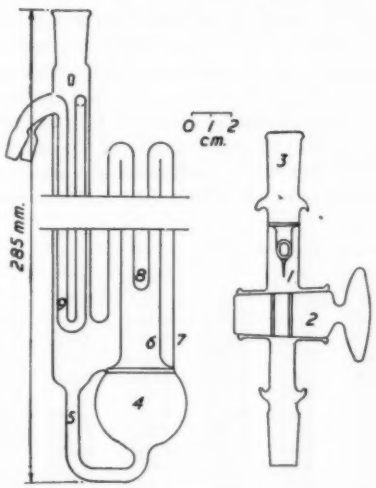
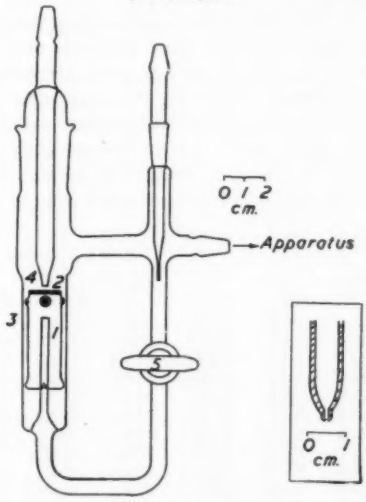


FIG. 2. *Cartesian manostat. Inset = pumping jet.*



the condensate was returned to the boiler through the narrow tube 5 which ensured rapid reheating of the condensate. A partial-immersion standard thermometer was used at its correct depth of immersion and a small quantity of mercury was required to make thermal contact between the thermometer and pocket 8. The alkoxide was made to boil under an atmosphere of nitrogen at a pressure which was read on the accurate manometer [1] and controlled by a manostat (Fig. 2) which operated on the Cartesian Diver principle. The diver 1 was just free to move in the jacket 3 and carried a Neoprene cushion 2 which closed the pump jet 4 at its ground orifice. Slight leakage through this valve was compensated by a controlled leak of nitrogen. Enough mercury was used to give a clearance of 1—2 mm. between the cushion and the jet during evacuation: this ensured rapid evacuation when the valve opened and only a small change in pressure was needed to shut the valve. By means of the tap 5 the manostat could be set to operate at the required pressure. Extensive tests proved that this manostat was far superior in sensitivity and stability over long periods to two other types which used valves employing mercury and sintered-glass discs. For example, the manostat showed fluctuations of 0·04 mm. at 2·3 mm. and 0·15 mm. at 42 mm. Hg each during an hour.

At a given pressure the steady readings of the thermometer (at 8) were recorded at several temperatures of the heating-bath in the vicinity of the true b. p. The thermometer readings were plotted as ordinates against the bath-temperatures as abscissæ and the curve showed a

plateau in which the thermometer temperature changed by less than 0·1° whilst the bath-temperature rose by 15°. The position of the plateau was independent of increasing or decreasing bath-temperature, but equilibrium was approached much more rapidly from the high-temperature end. The temperature of the plateau was recorded as the b. p.

Results and Discussion

Zirconium Tetra-tert.-*butoxide*.—The results are presented in Table 1 in which $P_{calc.}$ is the vapour pressure calculated from the equation:

$$\log P_{calc.}(\text{mm.}) = 51{\cdot}0296 - 5281{\cdot}72/T - 13{\cdot}9703 \log T \quad . \quad . \quad . \quad (1)$$

The values of P in parentheses and in italics were not used in computing this equation which was obtained by the laborious procedure already described.[1] Values in italics were determined by the hypsometer method and involved two different samples. The results by the static method were obtained from four different experiments, and the values in parentheses were excluded from the computation either because they were too low to be reasonably accurate or because they were subject to slight errors due to thermal decomposition.

For the 39 points used in computing the equation the coefficient of variation was $\pm 1{\cdot}8\%$, corresponding to a most probable error of a single point of $\pm 1{\cdot}2\%$. When these points are taken in order of ascending temperature irrespective of the number of the experiment (as shown in Table 1), the errors ($\Delta P = P - P_{calc.}$) show 26 changes in sign compared with the 20 required for random distribution of errors. Clearly, equation (1) represents these points well. In the low-pressure region 0·06—0·26 mm. (not computed) the observed pressures are more frequently lower than calculated, whilst the coefficient of variation is $\pm 0{\cdot}01$ mm. which is reasonable in view of the probable error of $\pm 0{\cdot}005$ mm. in the pressure

Table 1. *Zirconium tetra*-tert.-*butoxide*.

Temp. (K)	P (mm.)	$P_{calc.}$	Temp. (K)	P (mm.)	$P_{calc.}$	Temp. (K)	P (mm.)	$P_{calc.}$	Temp. (K)	P (mm.)	$P_{calc.}$
299·4°	(0·06)	0·06	308·6°	(0·12)	0·14	349·5°	2·40	2·424	403·8°	(35·37)	34·72
300·4	(0·07)	0·07	308·8	(0·13)	0·14	350·0	2·50	2·498	410·7	(46·00)	45·56
300·6	(0·07)	0·07	312·0	(0·16)	0·18	353·6	3·07	3·085	411·0	(46·29)	45·98
301·6	(0·08)	0·08	313·4	(0·20)	0·20	353·9	3·12	3·138	416·7	(56·94)	56·86
301·7	(0·07)	0·08	315·3	(0·20)	0·23	354·4	3·17	3·230	417·0	(57·67)	57·47
302·2	(0·08)	0·08	316·7	(0·24)	0·26	357·6	3·85	3·872	*417·3*	*58·10*	58·20
302·3	(0·08)	0·08	319·1	0·31	0·314	360·9	4·78	4·647	*418·7*	*61·10*	61·10
303·2	(0·08)	0·09	322·3	0·40	0·399	363·0	5·18	5·208	*420·2*	*62·80*	64·50
303·6	(0·10)	0·09	324·6	0·46	0·472	366·1	6·17	6·14	420·9	(67·14)	66·13
303·8	(0·09)	0·09	327·1	0·58	0·565	368·7	6·93	7·03	*423·4*	*71·00*	72·20
303·9	(0·09)	0·09	328·1	0·60	0·606	370·2	7·65	7·59	424·1	(73·83)	73·98
304·0	(0·09)	0·09	329·3	0·63	0·659	*374·8*	*9·46*	9·55	427·9	(85·95)	84·26
304·3	(0·09)	0·10	330·6	0·74	0·721	375·4	9·79	9·85	*431·8*	*94·90*	95·70
304·8	(0·09)	0·10	331·4	0·79	0·762	379·6	12·10	12·07	432·9	(101·1)	99·46
305·1	(0·09)	0·10	331·9	0·81	0·783	381·1	12·95	12·96	*439·9*	*124·1*	124·3
305·3	(0·10)	0·10	334·2	0·90	0·921	*383·7*	*14·42*	14·63	440·6	(129·0)	127·1
305·4	(0·10)	0·10	335·5	1·03	1·005	384·4	15·14	15·11	*448·1*	*159·7*	159·3
305·6	(0·10)	0·11	336·8	1·11	1·095	387·9	17·60	17·71	448·3	(162·6)	160·2
305·7	(0·10)	0·11	338·1	1·16	1·192	389·1	18·72	18·69	*454·0*	*192·2*	188·8
306·6	(0·10)	0·12	339·4	1·32	1·297	*392·6*	*21·67*	21·78	*457·0*	*216·3*	205·2
306·6	(0·11)	0·12	341·1	1·42	1·446	394·9	24·05	24·05	*457·9*	*215·3*	210·5
307·1	(0·12)	0·12	343·5	1·71	1·682	395·2	24·28	24·35	*477·6*	*372·4*	349·5
307·4	(0·12)	0·12	343·6	1·66	1·692	*402·3*	*32·49*	32·70	*480·9*	*412·3*	378·0
308·3	(0·13)	0·13	347·8	2·24	2·190	402·4	32·93	32·82	*486·3*	*464·6*	428·4
308·4	(0·12)	0·13	348·2	2·20	2·243						

measurements. The 11 pressures determined by the static method in the high-temperature region (403·8—448·3°) are predominantly higher than the calculated but in no case does the error exceed 2% and the coefficient of variation is $\pm 1{\cdot}3\%$. Considering now the results obtained by the hypsometric method, we find that the 4 points obtained in the " computed " region are in close agreement with the calculations based on equation

(1) which was computed from the static measurements. In fact, the agreement extends to higher pressures and the 11 points from 9·46 to 159·3 mm. gave a standard deviation of only ±1·1% although the observed pressures tended generally to be lower than the calculated. It seems reasonable to suggest that equation (1) is valid for calculations of the vapour pressures of zirconium tetra-*tert.*-butoxide in the pressure range 0·05—200 mm. Hg (300—450° K). Above ~450° K the observed pressures are considerably and increasingly higher than calculated and the spoon-gauge method showed that thermal decomposition becomes significant. Nevertheless, it is surprising that the hypsometer method gives such high results because non-volatile products of decomposition stay in the boiler (4) whilst the volatile products (olefin and alcohol) should diffuse out of the vapour and merely displace an appropriate volume of nitrogen through the manostat. Thus the thermometer is bathed in condensing vapour of alkoxide and, provided the manostat can cope with the volatile products of decomposition, the true boiling point should be measured. During the testing of the manostat we found that a deliberate leakage of nitrogen which could raise the pressure in the apparatus by 35 mm. Hg per min. (in the absence of the manostat) was dealt with efficiently by the manostat and caused a rise of only 0·3 mm. Hg in the apparatus. Hence it is possible that equation (1) should not be extrapolated above 450° K and that the vapour pressures determined hypsometrically are more accurate than the $P_{calc.}$ data imply.

In comparing these results on zirconium tetra-*tert.*-butoxide with those on the titanium derivative [1] it is clear that the zirconium compound is significantly the more volatile over the whole range of pressures studied.

TABLE 2. *Zirconium tetra*-tert.-*amyloxide.*

Temp. (K)	*P* (mm.)	$P_{calc.}$	Temp. (K)	*P* (mm.)	$P_{calc.}$	Temp. (K)	*P* (mm.)	$P_{calc.}$	Temp. (K)	*P* (mm.)	$P_{calc.}$
331·0°	(0·02)	$0·02_6$	343·6°	(0·06)	$0·07_6$	374·6°	0·73	0·71	406·4°	4·26	4·18
332·1	(0·03)	0·03	343·8	(0·06)	$0·07_7$	375·5	0·77	0·75	409·1	4·71	4·77
333·2	(0·03)	0·03	344·5	(0·07)	0·08	376·6	0·81	0·80	*409·4*	*4·85*	4·84
333·4	(0·03)	0·03	344·9	(0·07)	$0·08_5$	378·0	0·85	0·87	*409·5*	*4·86*	4·86
335·1	(0·03)	$0·03_7$	345·6	(0·08)	0·09	378·9	0·94	0·92	*410·3*	*5·02*	5·05
335·9	(0·03)	0·04	345·7	(0·08)	0·09	379·5	0·98	$0·95_6$	412·8	5·70	5·69
336·3	(0·03)	0·04	345·9	(0·08)	0·09	382·4	1·19	1·14	412·9	5·76	5·72
337·8	(0·04)	$0·04_2$	345·9	(0·08)	0·09	382·9	1·13	1·17	*413·4*	*5·79*	5·85
337·9	(0·04)	$0·04_7$	346·6	(0·08)	$0·09_7$	383·4	1·21	$1·21_4$	415·8	6·38	6·54
338·1	(0·04)	$0·04_8$	347·4	(0·08)	$0·10_3$	384·6	1·30	$1·29_6$	417·1	6·96	6·94
338·5	(0·03)	0·05	349·4	(0·11)	0·12	387·1	1·44	1·50	*419·4*	*7·67*	7·70
338·9	(0·04)	0·05	351·8	(0·14)	$0·14_5$	388·7	1·66	1·64	422·5	8·79	8·82
339·4	(0·04)	$0·05_4$	352·1	(0·15)	$0·14_8$	390·1	1·76	1·77	426·1	10·41	10·30
339·6	(0·04)	$0·05_5$	352·8	(0·14)	0·16	390·1	1·82	1·77	426·5	10·46	10·48
340·1	(0·05)	$0·05_7$	352·9	(0·15)	0·16	391·9	1·99	1·96	*428·6*	*11·47*	11·44
340·4	(0·04)	$0·05_9$	354·2	(0·17)	$0·17_4$	392·8	2·00	2·06	*431·5*	*12·96*	12·89
340·5	(0·04)	$0·05_9$	355·6	(0·18)	0·19	393·1	2·10	$2·09_6$	*432·0*	*13·35*	13·16
340·9	(0·05)	0·06	356·0	(0·20)	$0·19_6$	*394·7*	*2·28*	2·28	432·3	(13·28)	13·31
341·2	(0·04)	$0·06_3$	357·5	(0·21)	0·22	394·8	2·29	2·30	434·1	(14·58)	14·33
341·5	(0·06)	$0·06_4$	360·7	(0·27)	0·28	395·5	2·42	2·39	*434·3*	*14·68*	14·43
341·8	(0·05)	$0·06_6$	361·3	0·29	0·29	*396·4*	*2·45*	2·50	438·7	(17·24)	17·14
341·9	(0·05)	$0·06_6$	363·7	0·34	$0·34_3$	397·9	2·70	2·71	*439·5*	*18·14*	17·68
341·9	(0·05)	$0·06_8$	364·0	0·34	0·35	398·6	2·85	2·81	443·8	(22·11)	20·78
342·1	(0·06)	$0·06_7$	367·3	0·43	0·44	398·7	2·84	2·83	*447·4*	*25·02*	23·70
342·2	(0·06)	$0·06_8$	367·9	0·46	$0·45_7$	*400·0*	*3·02*	$3·02_6$	448·4	(25·60)	24·57
342·4	(0·05)	$0·06_9$	369·3	0·49	0·50	*401·1*	*3·16*	3·20	450·9	(28·82)	26·85
342·4	(6·06)	$0·06_9$	370·1	0·52	$0·52_8$	404·0	3·71	3·71	455·9	(33·93)	31·79
342·4	(0·06)	$0·06_9$	372·3	0·61	$0·60_9$	404·3	3·68	3·77	460·4	(40·65)	37·01
342·5	(0·06)	0·07				405·2	3·95	3·94	*461·3*	*41·70*	38·13
342·6	(0·05)	0·07							462·0	(42·42)	39·00

Zirconium Tetra-tert.-*amyloxide.*—The results for four runs by the static method and two by the hypsometric method are given in Table 2 in the same manner as for the *tert.*-butoxide in Table 1. Computation of the results of the static method in the pressure range 0·29—10·46 mm. gave the equation:

$$\log P \text{ (mm.)} = 78·7844 - 7566·42_3/T - 22·8232_8 \log T \quad . \quad . \quad . \quad (2)$$

The 42 computed results gave a coefficient of variation of $\pm 1{\cdot}7\%$ corresponding to a probable error for a single point of $\pm 1{\cdot}2\%$. Arranged in ascending order of temperature irrespective of the number of the run, the data give 27 changes of sign in error (ΔP) compared with 22 required for a random distribution of errors. The coefficient of variation for the uncomputed results (in parentheses) in the lower pressure region is $\pm 0{\cdot}014$ mm. and, as was found for the *tert.*-butoxide, the observed results tend to be lower than those calculated from equation (2). In the high-temperature region the static method gave good agreement with equation (2) up to about 440° K, but above this the observed pressures were considerably higher than calculated and thermal decomposition was detected. The hypsometric method gave results in the computed zone in good agreement with equation (2) and the 12 points had a percentage standard deviation of $\pm 0{\cdot}9\%$ with 6 negative errors (ΔP) and 4 positive. The agreement with equation (2) also extended beyond the upper limit of the computed zone to about 440° K, but at higher temperatures the pressures measured were considerably higher than calculated. It appears that equation (2) is valid for the calculation of vapour pressures for zirconium tetra-*tert.*-amyloxide over the pressure range 0·02—20·0 mm. Hg (330—440° K). Comparing these results with those on the corresponding titanium compound [1] shows that the zirconium compound is the more volatile in the region studied as was found in the case of the *tert.*-butoxides.

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151. *The Composition of the "Strong" Phosphoric Acids.*

By R. F. JAMESON.

A study of the composition of the "strong" phosphoric acids between the range 67·4—89·4% of phosphoric oxide has largely confirmed Parks and Van Wazer's reorganisation theory (based on a flexible chain model).[1] The ion-exchange chromatographic method used permitted separation of linear phosphoric acid polymers containing up to 14 phosphorus atoms in the chain, and some evidence for the formation of ring polymers was found in the solutions containing more than 86·1% of phosphoric oxide. The present results also indicate no essential change in the composition at the concentration of phosphoric oxide equivalent to $(HPO_3)_n$, *i.e.*, at 88·7%, and it is thus possible that the small-ring polymers found are only formed from more complicated ring and branched-chain polymers by hydrolysis during the preparation of the sample for analysis.

EQUILIBRIUM mixtures of phosphoric oxide and water containing more than 72·4% of phosphoric oxide, the so-called "strong" phosphoric acids,* have been shown by earlier workers [2] to be equilibrium mixtures of various linear polymeric species of the form $H_{n+2}P_nO_{3n+1}$. The first important attempt to analyse the mixtures was by Bell,[3] who used wet-chemical methods, but these methods are limited to very short chain-length polymers, up to the triphosphate. Paper chromatography has been employed by several workers,

* The term "strong phosphoric acids" used in this Paper has a special significance in that it refers to those mixtures of phosphoric oxide and water that contain more phosphoric oxide than is required for the formation of orthophosphoric acid, and does not refer to the concentration of hydrogen ion.

[1] Parks and Van Wazer, *J. Amer. Chem. Soc.*, 1957, **79**, 4890.
[2] Thilo, *Chem. Tech.* (*Berlin*), 1956, **8**, 251, and references therein.
[3] Bell, *Ind. Eng. Chem.*, 1948, **40**, 1464.

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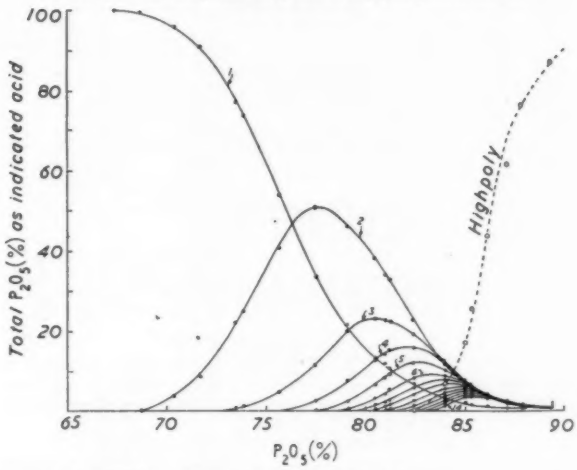
and a complete analysis by this method was given by Huhti and Gartaganis [4] covering the series up to nonaphosphoric acid.

Anion-exchange was developed by Beukenkamp, Rieman III, and Lindenbaum [5] and by Higgins and Baldwin,[6] and data for the system were also given by Ohashi and Sugatani.[7] The method has also been developed by Busch, Ebel, and Blanck [8] as a means of preparing samples of the free acids up to the octaphosphoric acid. The present work was carried out by using a gradient-elution technique, first proposed by Grande and Beukenkamp,[9] supplemented by ascending one- and two-dimensional paper chromatography.

Other methods that have been suggested include pH titration,[10] infrared spectroscopy,[11] *X*-ray diffraction,[12] and nuclear magnetic resonance,[13] the last three methods having the

FIG. 1. *The composition of the strong phosphoric acids.*



——●—— 1 = Ortho-; 2 = pyro-; 3 = tri-, etc.
---○--- Highpoly. = highly polymeric material hydrolysed from column.

advantage that the sample is not broken down before analysis, but at present they are relatively insensitive.

During the course of this work, Parks and Van Wazer,[1] using a flexible-chain model, calculated from theoretical considerations the distribution of polymers in the strong phosphoric acids. They assumed the polymers to be entirely of the linear type, and their results are in very close agreement with the present work, except that this work suggests the presence of more complicated structures above *ca.* 81% of phosphoric oxide.

Results.—The results of a series of analyses of the strong phosphoric acids are shown in Table 1 and Fig. 1. A typical elution curve is given in Fig. 2 in order that the degree of separation achieved and the method of estimating the 13th and 14th members of the series can be illustrated. Occasionally a 15th peak in the elution series of straight-chain

[4] Huhti and Gartaganis, *Canad. J. Chem.*, 1956, **34**, 785, and references therein.
[5] Beukenkamp, Rieman III, and Lindenbaum, *Analyt. Chem.*, 1954, **26**, 505; also Lindenbaum, Peters, and Rieman III, *Analyt. Chim. Acta*, 1954, **11**, 530, and Peters and Rieman III, *ibid.*, 1956, **14**, 131.
[6] Higgins and Baldwin, *Analyt. Chem.*, 1955, **27**, 1780.
[7] Ohashi and Sugatani, *Bull. Chem. Soc. Japan*, 1957, **30**, 864.
[8] Busch, Ebel, and Blanck, *Bull. Soc. chim. France*, 1957, 486.
[9] Grande and Beukenkamp, *Analyt. Chem.*, 1956, **28**, 1497.
[10] Van Wazer, Griffith, and McCullough, *ibid.*, 1954, **26**, 1755.
[11] Corbridge and Lowe, *ibid.*, 1955, **27**, 1383.
[12] Mabis and Quimby, *ibid.*, 1953, **25**, 1814.
[13] Callis, Van Wazer, and Shoolery, *ibid.*, 1956, **28**, 269.

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TABLE 1. *Composition of the strong phosphoric acids.*

Total P_2O_5 (%) *	$[P_2O_5]$ / $[H_2O]$	Percentage composition in terms of the constituent polyphosphoric acids.† 1	2	3	4	5	6	7	8	9	10	11	12	13	14	High-poly.	Tri-meta-	Tetra-meta-
67·4 [a]	0·263	100·0																
68·7 [a]	0·279	99·7	0·33															
70·4 [a]	0·302	96·2	3·85															
71·7 [a]	0·321	91·0	8·86	tr.														
73·5 [a]	0·352	77·1	22·1	0·79														
73·9 [b]	0·360	73·6	25·1	1·34														
75·7 [b]	0·394	53·9	40·7	4·86	0·46													
77·5 [a]	0·438	33·5	50·6	11·5	2·68	0·74	tr.											
79·1 [a]	0·481	22·1	46·3	20·3	7·82	2·26	1·02	0·34										
80·5 [b]	0·523	13·8	38·2	23·0	13·0	6·86	3·38	1·67	1·03	0·22								
81·0 [b]	0·542	12·2	34·0	22·7	14·6	8·42	4·36	2·27	1·41	0·56	tr.							
81·2 [b]	0·549	10·9	32·9	22·3	15·0	9·36	5·41	2·85	1·75	0·97	0·36	0·05						
82·4 [a]	0·594	7·32	23·0	19·3	15·9	12·3	8·21	5·73	3·89	2·52	1·36	0·91	0·14			tr.		
84·0 [a]	0·667	3·92	11·8	12·7	12·0	10·5	8·97	7·99	6·62	5·63	4·54	3·72	3·03	2·46	1·68	6·63		
85·0 [b]	0·717	2·28	6·36	7·32	8·01	8·17	7·67	7·22	6·93	6·42	5·89	5·27	4·69	3·99	3·83	16·9		
85·3 [a]	0·736	1·87	4·73	6·33	6·58	6·66	6·71	6·36	6·11	5·88	5·46	5·07	4·90	4·64	4·38	25·6		
86·1 [b]	0·787	1·46	2·81	3·74	4·43	4·52	4·77	4·79	4·93	4·67	4·54	4·67	4·63	4·38	4·17	43·5	0·17	
87·1 [b]	0·860	0·83	1·81	2·17	2·53	3·09	3·39	3·46	3·33	3·55	3·47	3·45	3·52	3·26	3·24	61·1	tr.	
87·9 [b]	0·920	0·50	0·82	1·56	1·76	1·72	2·03	2·13	2·26	2·07	2·26	2·06	2·20	1·99	2·30	76·4	0·42	0·11
89·4 [b]	1·066	1·88	1·52	0·77	0·61	0·62	0·68	0·54	0·71	0·86	1·03	0·98	1·16	1·23	1·37	86·8	1·17	0·41

* [a] Prepared by dehydration of orthophosphoric acid; [b] prepared by dissolving phosphoric oxide in orthophosphoric acid.

† 1 = Ortho-, 2 = pyro-, 3 = tri-, 4 = tetra-phosphate, etc.; highpoly. = material retained by resin and includes the 15-phosphoric acid when this was separated.

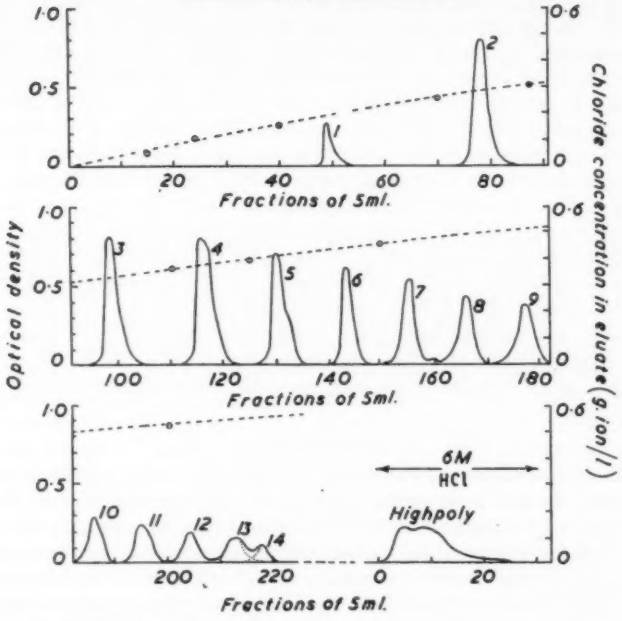
TABLE 2. *Composition of the hydrolysis products of the highly polymeric phosphates retained by the resin, analysed by paper chromatography.*

Total P_2O_5 (%)	Constituent acids (%) Ortho-	Pyro-	Trimeta-	Tetrameta-
84·0	95·2	4·8	—	—
85·0	86·8	12·8	0·4	tr.
85·3	93·7	6·3	tr.	—
86·1	82·2	17·2	0·5	0·1
87·1	84·3	15·3	0·4	tr.
87·9	86·4	12·6	0·9	0·1
89·4	80·7	16·6	2·3	0·4

TABLE 3. *Eluting solutions (quantities for* 1 *l. of solution).*

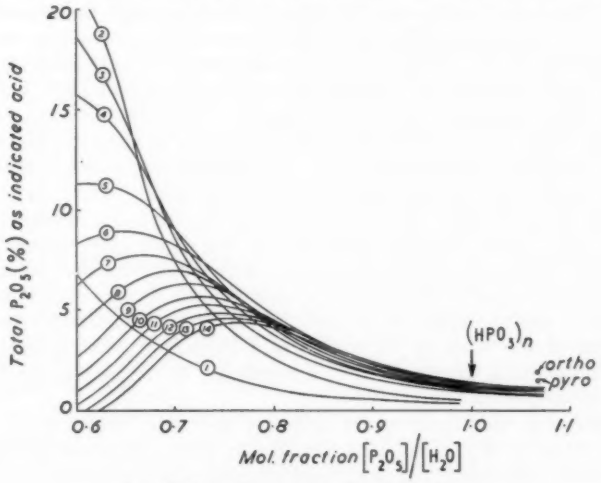
Solution	Potassium chloride (g.)	Potassium formate (g.)	Formic acid (ml.)	25% Aqueous ammonia
(i)	74·5	6·3	2·5	Until the pH = 5·5
(ii)	63·4	5·5	2·0	
(iii)	55·8	4·2	2·0	

FIG. 2. *A typical elution curve.*



1 = Ortho-; 2 = pyro-; 3 = tri-, etc.
———— % of P_2O_5 in terms of optical density (molybdenum blue; 830 mμ).
---O--- chloride content of eluate (g.-ion/l.), theoretical curve and experimental points.

FIG. 3. *Variation of the composition of the strong phosphoric acids with the mol. fraction* $[P_2O_5]/[H_2O]$.



1 = Ortho-; 2 = pyro-; 3 = tri-, etc.
Experimental points omitted for clarity.

polymers was obtained, but in general, a sharp cut-off in the series occurred at a chain length of 12—14 phosphate units according to the resin used. Higher polymers required hydrolysis on the column with 6M-hydrochloric acid before they could be eluted.

The result indicated by Huhti and Gartaganis,[4] namely, that the concentration of all the lower polymers tend to zero at the composition representing $(HPO_3)_n$, *i.e.*, 88·7% of phosphoric oxide, is not supported. In fact, the results show no discontinuity at this point, as is illustrated in Fig. 3. However, the possibility that the lower chains indicated at these high concentrations of phosphoric oxide are only produced during the preparation of the sample for analysis or on the column by hydrolysis cannot be ruled out.

Occasionally the ring polymer trimetaphosphoric acid (I) appeared in the elution series, and sometimes a trace of tetrametaphosphoric acid (II) was indicated (Table 1). Since, however, hydrolysis on the column of the highly polymeric material obtained above about 82·4% of phosphoric oxide led to the formation of these compounds (paper chromatography of the eluate, Table 2) it is probable that they are not present in the form of simple compounds, but are the hydrolysis products of more complex compounds. The relatively high concentration of ortho- and pyro-phosphoric acids found in the solution containing 89·4% of phosphoric oxide also suggests fairly extensive hydrolysis of this material (Table 1).

Discussion

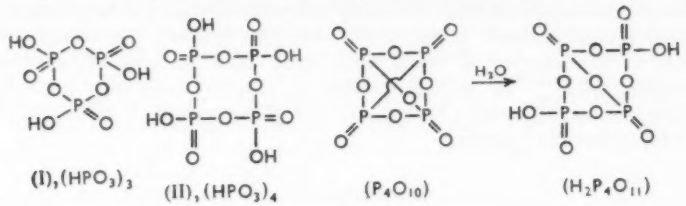
Nature of the Elution Curves.—The sharp cut-off in the elution series at the 12—15th member is almost certainly a molecular-sieve effect as suggested by Van Wazer.[14] The gradient-elution technique used in this work would be expected to enhance any such effect, as it causes continual shrinkage of the resin as the run proceeds and also cuts the amount of " tailing " of each fraction. Further support is also obtained from the fact that the cut-off varies with the type of resin used, and this probably explains why Ohashi and Sugatani [7] failed to find evidence for more than the tetraphosphoric acid in their work.

Nature of the Strong Phosphoric Acids.—The present results support the conclusions of earlier workers [2-4] in indicating that the composition of the strong phosphoric acids is a function of the phosphoric oxide concentration and not of the method of formation, the solutions having been prepared both by concentrating orthophosphoric acid by evaporation and by dissolving anhydrous phosphoric oxide in syrupy phosphoric acid. Contrary to the work of Huhti and Gartaganis,[4] the present work suggests that the formula $(HPO_3)_n$ has no physical or chemical significance. The former authors show that the concentration of the lower members of the series, up to the nonaphosphoric acid, tends to zero at 88·7% of phosphoric oxide, whereas the results shown in Table 1 and Figs. 1 and 3 suggest a persistence of these polymers beyond this point. Thus the formula $(HPO_3)_n$ cannot represent the presence of only extremely long polymers of the type $H_{n+2}P_nO_{3n+1}$ where $n \longrightarrow \infty$, but must be a mixture that also contains more complex structures. Also the presence of tri- and tetra-metaphosphoric acids in the solutions of high phosphoric oxide content and in the hydrolysis products of the highly polymeric species retained by the resin suggests that these complex materials are based on ring-containing compounds. Thilo and Sauer,[15] using paper chromatography, have also shown that materials containing more than 90% of phosphoric oxide give rise to substantial quantities of trimetaphosphoric acid and traces of tetrametaphosphoric acid. Further evidence for the continuity of the system is found in the work of Tarbutton and Deming,[16] who show that the system phosphoric oxide–water is azeotropic with a maximum in the boiling point occurring at a concentration of 92% of phosphoric oxide.

The complex ring compounds could arise *via* two main mechanisms: either by the partial hydrolysis of the P_4O_{10} molecule, perhaps by long-chain acids instead of by water, or by extensive cross-linking of the linear and branched chain polymers.

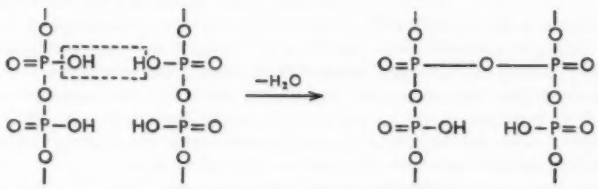
[14] Van Wazer, personal communication.
[15] Thilo and Sauer, *J. prakt. Chem.*, 1957, **4**, 324.
[16] Tarbutton and Deming, *J. Amer. Chem. Soc.*, 1950, **72**, 2086.

The hydrolysis of phosphoric oxide probably follows the scheme:



the next stage resulting in the formation of either a six-membered trimetaphosphate ring or an eight-membered tetrametaphosphate ring, according to which P–O–P link is next to be broken (of the five P–O–P links, four of them are identical, and any one of these will give the trimetaphosphate ring on hydrolysis, whereas the fifth and more anhydrous link will give the tetrametaphosphate product). The actual ratio of tri- to tetra-metaphosphate produced in such a reaction would be difficult to obtain as the greater stability of the trimetaphosphate ring makes its detection easier. The amount of "free water" in the concentrated solutions is very low (Parks and Van Wazer,[1] Huhti and Gartaganis,[4] and Ohashi and Sugatani [7]) and it could thus well be that the hydrolysis is effected by long-chain phosphoric acids instead of by water, leading to the formation of even more complex compounds. The first stages of the hydrolysis would thus give rise to extremely unstable compounds containing more phosphoric oxide than is permitted by the formula $(HPO_3)_n$, although their presence cannot be demonstrated by any method that involves dilution of the original material. That they exist is suggested, however, by the presence of their hydrolysis products and by the work of Brown and Whitt [17] on the vapour phase. These authors concluded that the vapour above the strong phosphoric acids consists mainly of P_4O_{10} molecules with some water vapour, basing their conclusions on vapour-density measurements made at 1020°, but the relatively high temperature employed could have led to considerable dissociation. It seems highly improbable that the P_4O_{10} molecules would dissolve unchanged, especially in the more dilute solutions.

It has been suggested by Thilo and Sauer [15] that cross-linking of the long-chain polymers can take place as follows:



this reaction leading to the formation of compounds in the form of a large three-dimensional network, and with the required high phosphoric oxide content. It is believed that any side-chain polymers that might be formed in this way would defy detection by methods such as have been employed here (Van Wazer and Holst [18]), but extensive cross-linking might well lead to the formation of the more stable tri- and tetra-metaphosphate rings, which could be detected. However, as Thilo and Sauer [15] have pointed out, hydrolysis of such materials would also give rise to high results for linear polymers of intermediate chain-length, and this effect has not been noted either in this work or in that of Huhti and Gartaganis.[4] This mechanism would also seem less likely to lead to a system in which the vapour had only a very low concentration of polymeric acids, but a

[17] Brown and Whitt, *Ind. Eng. Chem.*, 1952, **44**, 615.
[18] Van Wazer and Holst, *J. Amer. Chem. Soc.*, 1950, **72**, 639.

high concentration of unchanged P_4O_{10} molecules (Brown and Whitt [17]), although extrapolation of these data (at 1020°) to room temperature may not be justified.

In the lower concentration range, Parks and Van Wazer's theoretical calculations [1] would appear to be confirmed, in many cases better than has been shown previously by paper chromatography.[4,7] In the higher range the inherent experimental error makes the deviation insignificant, although a certain amount of discrepancy is to be expected on the basis of the ideas discussed above.

Experimental

Preparation of the Acids.—Two methods were used to prepare the strong phosphoric acids: (*a*) Samples of " AnalaR " orthophosphoric acid were dehydrated by heating to temperatures up to 400° in a platinum crucible and then allowed to cool in a vacuum-desiccator (without desiccant) and left for 5—10 days before analysis, and (*b*) anhydrous phosphoric oxide was dissolved in " AnalaR " phosphoric acid to give the required mixture and heated in order to obtain a uniform melt, the sample then being allowed to cool as in (*a*).

The higher acids became opaque and crystallised when kept for longer periods, but only the one-phase syrups or glasses were analysed in order to circumvent any complications that may have arisen when more than one phase was present. The method used for each sample is indicated in Table 1.

Preparation of the Solutions for Analysis.—The acid was first cooled to −5° and then, by means of a glass rod, a small quantity was removed and dissolved in about 10 ml. of ice-cold 0·5M-sodium hydroxide solution. The final mixture was alkaline to phenolphthalein. A further weighed quantity of the acid was hydrolysed to orthophosphoric acid by boiling with 0·3M-perchloric acid, and the total phosphate (in terms of phosphoric oxide, P_2O_5) estimated by titration of a suitable aliquot portion with bismuthyl perchlorate (see below).

Paper Chromatography.—Ebel's two-dimensional technique [20] and Huhti and Gartaganis's ascending method [4] were employed. The solvents were those described by Ebel [20] and specially treated Whatman No. 1 chromatographic paper was used. The paper had first been washed with a 3% solution of EDTA (disodium salt) and then several times with distilled water and dried. This treatment was necessary in order to remove traces of alkaline-earth metals from the paper as these cause serious streaking of the chromatogram by forming complexes with the polyphosphoric acids and with the paper.

Preparation of Resins.—The resins used in the chromatographic analyses were of the strongly basic, quaternary ammonium type and two main varieties were used: (*a*) De-Acidite FF with a water regain of 1·36 g. per g. of the chloride form, and (*b*) De-Acidite FF with a water regain of 1·66. Both resins were of 100—200 mesh and were specially supplied by the Permutit Company Ltd. Resin (*b*) gave the best results except for the very concentrated acids, as these required a stronger eluting solution (see below) which caused too pronounced a shrinking of the resin. Resins with higher water-regains were also tried but the extensive shrinkage and tendency to break up into finer particles during a run made them impracticable. Another resin, Amberlite C.G. 400-I, was also used, but was not so efficient in separating the higher members, and the elution series usually terminated at about the 11th member.

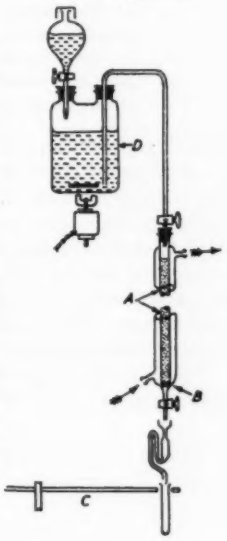
The resins were first washed with 6M-hydrochloric acid and then with distilled water. The column was then filled with a slurry of the resin in water, and a 1 m. long extension tube of the same diameter as the column was fitted. The column was then back-washed with distilled water at such a rate as to allow the " fines " to be run off the top of the tube. After removal of the " fines," the back-washing was discontinued, and the resin allowed to settle. The extension tube was then removed and the water-level adjusted so as to be just above the resin; the column was then ready for use. This treatment was repeated after every run, since the resin shrank considerably as the run progressed, and the 6M-hydrochloric acid used to complete each separation caused the resin to break up a little.

Ion-exchange Chromatography.—The apparatus employed is illustrated in Fig. 4. The columns (*A*) were 75 cm. long and 12 mm. in diameter and fitted with a water-jacket, the resin being supported on a sintered-glass disc (*B*). The fraction collector (*C*) was of the conventional siphon-pipette type, and fractions of 5 or 10 ml. were collected and analysed as outlined below.

A sample of the alkaline test solution, prepared as described above, was introduced by means of a weight-burette to the top of the column, the total phosphate thus added

being estimated by analysing another weight-fraction by the colorimetric method described below—not more than 5 mg. of phosphoric oxide were added for each run. The level of the liquid in the column was lowered to the level of the resin, 2 ml. of water added, and the level again adjusted, this procedure being carried out three times. It was necessary to keep the column at about 15° in order to get the best separation, and this was conveniently achieved by circulating tap-water around it. Temperatures of above 30° caused rapid hydrolysis, and below 15° the rate of flow through the column became too low. Lack of temperature control resulted in uneven heating (*e.g.*, by sunlight) and consequent poor separation of the bands.

FIG. 4. *Apparatus.*



The run was then commenced with 1 l. of water in the mixing-chamber (*D*) (stirring by means of a magnetic stirrer) and one of the three solutions given in Table 3 in the reservoir: solution (i) for mixtures initially containing more than 84% of phosphoric oxide, solution (ii) for those containing 80—84% of phosphoric oxide, and solution (iii) for those containing less than 80% of phosphoric oxide. Thus, as the run proceeded, so the strength of the elution solution increased (Fig. 2). There was no necessity to collect the first 150 ml. of eluate (see Fig. 2).

The elution was completed in each case with 6M-hydrochloric acid which was kept overnight in the column before the run was completed, thus enabling any highly polymeric material to be hydrolysed (mainly to ortho- and pyro-phosphoric acids, but some ring compounds survived this low-temperature hydrolysis, see Table 2) and removed from the column. Heating the column during this stage was disadvantageous as it caused complete hydrolysis to orthophosphate, thus preventing any information regarding the structure of the highly polymeric acids being obtained, and also increased the extent of the decomposition of the resin, and so was abandoned. About 0·1 ml. samples of the hydrolysate were examined by means of paper chromatography, and the amounts of the component phosphates recorded in Table 2.

Analysis.—Each fraction was hydrolysed by boiling dilute sulphuric acid, and the phosphoric oxide content estimated by Bolz and Mellon's method,[21] based on the hydrazine reduction of phosphomolybdate, optical densities being measured in 1-cm. glass cells at 830 mμ in a "Unicam" spectrophotometer and converted into mg. of phosphoric oxide by means of a calibration graph.

Paper chromatograms were first sprayed with a molybdate solution of the type recommended by Hanes and Isherwood,[22] and the spots then brought up by exposure to ultraviolet light. For quantitative work, the spots were then cut out and the phosphate leached out with ammonia solution and estimated as above; other portions of the same sheet were used in order to obtain a blank correction.

The phosphoric oxide contents of the original polyphosphoric acid mixtures were estimated, after hydrolysis with perchloric acid (see above), by the method of Salmon and Terrey [19] (titration with bismuthyl perchlorate with thiourea as indicator).

Occasional checks on the chloride content of the eluate were made and compared with the calculated values (Fig. 2).

Thanks are due to Dr. A. E. Scott for many helpful discussions during the course of this work, and to The Permutit Company Ltd. for gifts of the resins.

QUEEN'S COLLEGE (UNIVERSITY OF ST. ANDREWS), DUNDEE. [*Received, September 16th*, 1958.]

[19] Salmon and Terrey, *J.*, 1950, 2813.
[20] Ebel, *Bull. Soc. chim. France*, 1953, 998, 1085, 1089.
[21] Bolz and Mellon, *Ind. Eng. Chem. Anal.*, 1947, **19**, 873.
[22] Hanes and Isherwood, *Nature*, 1949, **164**, 1107.

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152. *Acyl Migration in Diglycerides.*

By A. Crossley, I. P. Freeman, B. J. F. Hudson, and J. H. Pierce.

1 : 2- or 1 : 3-Diglycerides, under the influence of heat or in the presence of catalysts, give an equilibrium mixture of the two esters. The effects of temperature and of the substituent acyl groups on the speed of migration have also been studied, and the work has been extended to monoglycerides.

The facility of acyl migration and the high proportion of the 1 : 2-isomers (which can, in most cases, be readily isolated) in the equilibrium mixture are of significance in the synthesis of diglycerides and their further conversion into triglycerides of known configuration. The application to the preparation of pure unsaturated 1 : 2-diglycerides is of particular interest.

Partial glycerides can be converted under certain conditions into isomers or into mixtures of isomers by migration of the acyl groups within the molecule. This has been studied for monoglycerides, *e.g.*, by Verkade and Lohuizen [1] and Martin,[2] but few workers have studied diglycerides. An early report by Grün [3] described the partial conversion of 1 : 3-distearin and 1 : 3-dipalmitin into the 1 : 2-isomers but most workers have been concerned with the change from 1 : 2- to 1 : 3-diglycerides during reaction and it appears to have been assumed that the 1 : 3-diglycerides are inherently more stable.[4] Our interest was aroused when syntheses of triglycerides from 1 : 3-diglycerides yielded products containing the asymmetrical triglycerides as well as the desired symmetrical isomers.

Equilibrium between 1 : 2- *and* 1 : 3-*Diglycerides.*—The work has been facilitated by the recent development of differential thermal analysis. This technique, which has recently

Table 1. *Melting points and equilibrium conditions for diglycerides* (3 *hours' heating*).

		M. p.		Equilibrium mixture	
		Chilled melt (D.T.A.*)	Crystals from solvent (capillary)	Heating temp.	1 : 3-Diglyceride (%)
Distearin	1 : 2	60·5°	68·0°	165°	58
	1 : 3	80·2	80·2		
Dipalmitin	1 : 2	*	62·8	<165	56
	1 : 3	*	73·2		
Dimyristin	1 : 2	*	55·5	<165	~55
	1 : 3	*	65·2		
Dilaurin	1 : 2	21·8	40·8	140	55
	1 : 3	57·7	57·7		
Diolein	1 : 2	−23·9 / −13·9	1·9 †	165	53
	1 : 3	25·8	25·8		
Glycerol di-*p*-nitrobenzoate	1 : 2	*	Liquid	160	~60
	1 : 3	*	138		

* Not determined. † Determined by D.T.A. after tempering.
* D.T.A. = differential thermal analysis.

been used in the study of fats,[6] depends on the measurement of temperature differences between a control cell and a cell containing a fat, as heat is applied at a constant rate to the system. If the temperature difference is plotted as a function of time over the range within which melting takes place both endothermal effects due to melting and exothermal

[1] Verkade and Lohuizen, *Proc. k. ned. Akad. Wetenschap.*, 1953, **56**, 324.
[2] Martin, *J. Amer. Chem. Soc.*, 1953, **75**, 5483.
[3] Grün, in Hefter-Schönfeld, "Chemie und Technologie der Fette und Fetteprodukte," Springer, Vienna, 1936, Vol. I, p. 250.
[4] Malkin and Bevan, "Progress in the Chemistry of Fats and Other Lipids," Pergamon, London, 1957, Vol. IV, p. 69; Gunstone, "An Introduction to the Chemistry of Fats and Fatty Acids," Butterworths, London, 1958, p. 89; Deuel, "The Lipids," Interscience, London, 1951, Vol. I, p. 170.
[5] Young and Sallans, *J. Amer. Oil Chemists' Soc.*, 1958, **35**, 392.
[6] Haighton and Hannewijk, *ibid.*, p. 344; Lavery, *ibid.*, p. 418.

effects due to polymorphic transformations are observed. Some curves for the distearins are shown in Fig. 1. 1 : 3-Distearin is characterised by a single sharp endothermic effect on melting (Fig. 1*a*). Heating at 165° gave a second component, and the curve showed two endothermic deflections. Fig. 1*c* shows the result of heating for ½ hr. Little change

FIG. 1. (*a*) 1 : 3-*Distearin.* (*b*) 1 : 2-*Distearin.* (*c*) *Migration product* (½ *hr.*) *at* 165°. (*d*) 1 : 2-*Distearin* 43%, *plus* 1 : 3-*distearin* 57%.

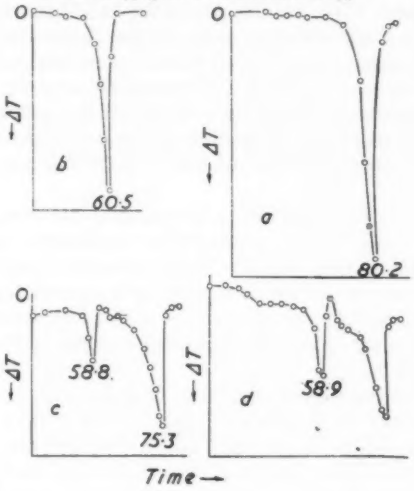
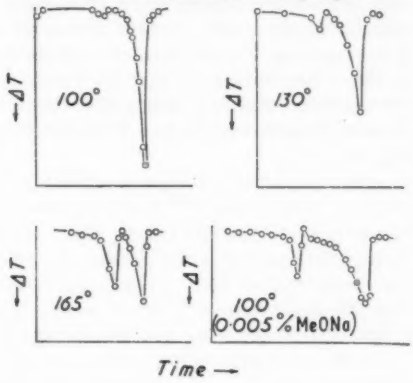


FIG. 2. 1 : 3-*Distearin heated for* ½ *hr.*



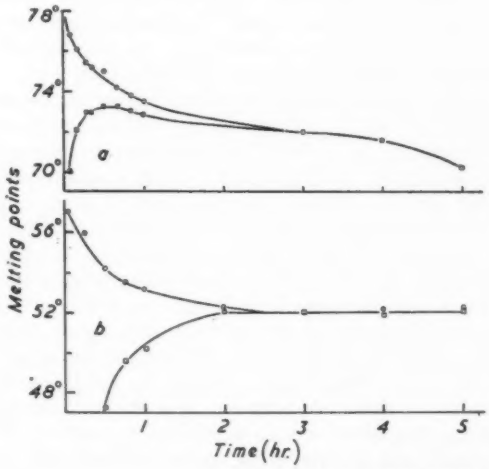


FIG. 3. *Acyl migration in diglycerides.*
○—○ (*Upper branch*) 1 : 3-*Diglycerides.*
□—□ (*Lower branch*) 1 : 2-*Diglycerides.*
(*a*) *Distearin at* 165°.
(*b*) *Dilaurin at* 140°.

FIGS. 1 & 3. *Differential thermal analysis.*

occurred as a result of further heating. 1 : 2-Distearin (Fig. 1*b*) showed a similar effect, forming apparently the same final mixture. These mixtures were each resolved by crystallisation from light petroleum into two components which were identified as 1 : 2- and 1 : 3-distearin. Starting from 1 : 3-distearin yielded 58·1% of 1 : 3-distearin and 41·9% of 1 : 2-distearin. From 1 : 2-distearin the yields were 58·2% and 41·7% respectively. Mixing 1 : 2- and 1 : 3-distearin in these proportions afforded a curve (Fig. 1*d*) very similar

to those of the heated samples, and this did not change appreciably on heating. It is evident that an equilibrium mixture of 1 : 2- and 1 : 3-distearin had been established.

The formation of an equilibrium mixture was also demonstrated by a study of the change in melting points on heating. In Fig. 3*a* these are recorded for the distearins and it can be seen that at 165° equilibrium is attained finally after about 3 hours. However, there is then a continued slow fall in melting point: this is thought to be due to true interesterification, or possibly to disproportionation as small amounts of monoglyceride can be detected analytically after several hours' heating. The time required for equilibration depends on the temperature of heating. Only slight changes occur in the differential thermal analysis curves of the distearins when heating was at temperatures below 165° for ½ hr. (see Fig. 2), but slow changes in melting point are evident at temperatures as low as 80°. The rate of change at these low temperatures is increased considerably by the presence of catalysts, either basic (*e.g.*, sodium hydroxide or methoxide) or acidic (*e.g.*, toluene-*p*-sulphonic acid). These are effective at concentrations of less than 0·005% (see Fig. 2).

Acyl migration has been studied thus with distearins, dipalmitins, dimyristins, dilaurins, dioleins, and glycerol di-*p*-nitrobenzoates (see Table 1). It appears that equilibrium is attained more readily the shorter the acyl radical (see Fig. 3*b*): the distearins reach equilibrium after 3 hours' heating at 165°, whereas the dilaurins need only be heated for the same time at 140°. This suggests that the short-chain diglycerides such as diacetin and dibutyrin may well be extremely labile. On the other hand, unsaturation has little effect, diolein behaving in a similar way to distearin.

In the aromatic field glycerol 1 : 3-di-*p*-nitrobenzoate was studied as its crystallisation behaviour was more satisfactory than that of the 1 : 3-dibenzoate. The 1 : 3-di-*p*-nitrobenzoate (m. p. 138°), when heated at 160°, showed an asymptotic fall in melting point to about 127°, but, as the corresponding 1 : 2-diglyceride could not be isolated as a solid, evidence of acyl migration in this case remains presumptive. The 1 : 3-diglyceride could be kept at 110° for six days without change in melting point: this implies a greater stability in aromatic than in aliphatic diglycerides, or, alternatively, as the aromatic diglyceride is solid at 110°, that acyl migration takes place only in the liquid state.

A question of interest in synthetic work is the extent to which acyl migration occurs in solution. The system in which hydrogen chloride is present is of particular importance as this has been widely used in the preparation of 1 : 3-diglycerides from 1-triphenylmethyl-2 : 3-diglycerides.[4,7] Conditions analogous to those used in this reaction were reproduced by passing hydrogen chloride through ethereal solutions of 1 : 3- and 1 : 2-distearin at room temperature. After 1 hour the diglycerides were recovered and in each case mixtures were obtained of similar composition to the equilibrium mixtures occurring in the molten state. It is apparent, therefore, that the hydrolysis of 1-triphenylmethyl-2 : 3-diglycerides with hydrogen chloride or similar reagents will result in a mixture of isomers. In a homogeneous system this would contain *ca.* 40% of the 1 : 2-isomer. However, the higher saturated diglycerides are precipitated during the reaction and the system is therefore "directed" in favour of the less soluble isomer, *i.e.*, the 1 : 3-diglyceride. This explains the yields of *ca.* 80% recorded for these compounds.[7] For the unsaturated diglycerides and the lower saturated diglycerides, which remain in solution throughout the reaction, this directing effect will not operate and low yields are to be expected, and, in fact have been reported for dilaurin and dicaprin.

It thus appears probable that the formation of 1 : 3-diglyceride from 1-triphenylmethyl-2 : 3-diglyceride proceeds *via* the 1 : 2-diglyceride which then undergoes acyl migration. Direct formation of 1 : 3-diglyceride from the triphenylmethyl compounds is not excluded by the present work but seems unlikely.

Acyl Migration as a Method of Preparing 1 : 2-*Diglycerides.*—Until recently the preparation of pure samples of diglycerides, especially 1 : 2-diglycerides, had been tedious.

[7] Verkade, van der Lee, and Meerburg, *Rec. Trav. chim.*, 1935, **54**, 716.

It has now been found that a 1 : 2-diglyceride may be isolated readily from an equilibrium mixture prepared by heating the 1 : 3-diglyceride. The separation depends on the great difference in solubility between the two isomers in light petroleum. Thus from a solution of the equilibrium mixture from 1 : 3-distearin in light petroleum, when cooled to 35°, 1 : 3-distearin, m. p. 79·3°, is precipitated and on further cooling of the filtrate, to 0°, 1 : 2-distearin, m. p. 68°, separates.

Classical methods of preparing 1 : 2-diglycerides depend on the removal, by hydrogenolysis, of protecting groups at the 3-position, as the final stage of the synthesis.[8] This technique is not applicable to the preparation of unsaturated diglycerides and until very recently no method of preparing such compounds was known. Baer and Buchnea[9] recently described the synthesis of D- and L-1 : 2-diolein by a method depending on the reductive debenzylation of optically active glycerol 1 : 2-di-(9 : 10-dibromostearate) 3-benzyl ethers followed by regeneration of the *cis*-double bonds in the diglyceride by the action of zinc in ether. Melting points of the products were not given but identification

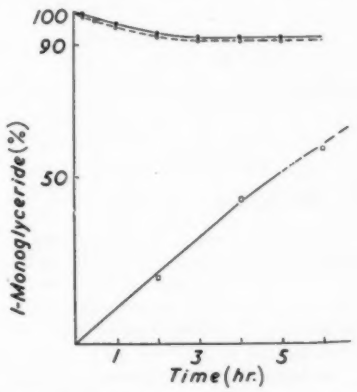


FIG. 4. *Acyl migration in monoglycerides at 100°.*

●—● (*Top curve*) 1-*Mono-olein.*
○ - - - ○ (*Middle curve*) 1-*Monostearin.*
□—□ (*Lower curve*) 2-*Monostearin.*

was by catalytic hydrogenation to D- and L-2 : 2-distearin. Acyl migration has provided a simpler alternative for the preparation of optically inactive 1 : 2-diolein and seems to be the only feasible route for the polyunsaturated 1 : 2-diglycerides.

Acyl Migration in Monoglycerides.—Our studies of pure monoglycerides have been less detailed than those of diglycerides. They show, however, that migration can be induced merely by heat. The rate of conversion of pure 1- or 2-monoglycerides into equilibrium mixtures was followed by analysis for 1-monoglyceride by the periodate method.[10] To ensure that only acyl migration, and not disproportionation, occurred, the total monoglyceride was also determined, by the method of Brokaw *et al.*[11] The results are shown in Fig. 4. Equilibrium mixtures containing about 90% of 1-monoglyceride are formed from pure 1-monostearin or 1-mono-olein in about 3 hours at 100°. Limited studies on the migration in the reverse direction indicate that it is much slower and is incomplete even after 6 hours' heating.

EXPERIMENTAL

Preparations of Saturated 1 : 3-*Diglycerides.*—These were prepared from the corresponding triglycerides by a method basically that of Baur and Lange[12] in which the diglyceride is preferentially crystallised from an interesting mixture of triglyceride, triacetin, and glycerol with sodium methoxide as catalyst. However, instead of destroying the catalyst with acetic acid the reaction mixture was ground to a paste with water. When this paste was then warmed,

[8] Verkade, Cohen, and Vroege, *Rec. Trav. chim.*, 1940, **59**, 1123.
[9] Baer and Buchnea, *J. Biol. Chem.*, 1958, **230**, 447.
[10] Handschumaker and Linteris, *J. Amer. Oil Chemists' Soc.*, 1947, **24**, 143.
[11] Brokaw, Perry, and Lyman, *ibid.*, 1955, **32**, 194.
[12] Baur and Lange, *J. Amer. Chem. Soc.*, 1951, **73**, 3926.

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the diglyceride separated as a molten layer. After being washed twice with water the crude diglyceride was crystallised from ethanol. This modified procedure was adopted as it was found that the original process left traces of sodium methoxide in the product which were sufficient to catalyse acyl migration as described above; in some cases the alkali was only removed after repeated washing of a hexane solution of the diglyceride with water. Our products obtained had the annexed characteristics.

		OH value				OH value	
	M. p.	Found	Calc.		M. p.	Found	Calc.
1 : 3-Distearin ...	80·0°	90·0	89·9	1 : 3-Dimyristin...	65·5	110·0	109·6
1 : 3-Dipalmitin ...	73·2	98·1	98·8	1 : 3-Dilaurin	58·0°	122·7	123·0

Preparations of Saturated 1 : 2-*Diglycerides.*—1 : 2-Distearin and 1 : 2-dilaurin were prepared by Howe and Malkin's method,[13] hydrogenolysis of the 2 : 3-di-*O*-acylglycerol 1-benzyl ether with palladium black as catalyst giving 1 : 2-distearin, m. p. (capillary) (α) 60·5°, (β) 68·0° (Found: OH value, 90·0. Calc.: OH value, 89·9), and 1 : 2-dilaurin, m. p. (capillary) (α) 20·0°, (β) 39·2° (Found: OH value, 122·5. Calc.: OH value, 123·0).

		Yield	I value	
Monoglyceride	M. p.	(%)	Found	Calc.
1-Mono-olein	35·5°	98·7	70·7	71·4
1-*p*-Nitrobenzoate	108·0	95·0	—	—

		OH value		I value	
Diglycerides	M. p.	Found	Calc.	Found	Calc.
1 : 3-Diolein	25·8°	90·2	90·5	81·4	81·9
1 : 3-Di-*p*-nitrobenzoate	138·0	142·6	143·8	—	—

Preparation of Other 1 : 3-*Diglycerides.*—1 : 3-Diolein and 1 : 3-di-(*p*-nitrobenzoyl)glycerol were prepared from the monoglycerides and acid chlorides by the method of Malkin, Shurbagy, and Meara.[14] The monoglycerides were prepared by the method of Daubert, Fricke, and Longenecker [15] from the acid chlorides and *iso*propylideneglycerol. See annexed Table.

Preparation of 1 : 2-*Diglycerides from* 1 : 3-*Diglycerides by Isomerisation.*—The 1 : 3-diglycerides were heated at 165° for 1 hr. (under nitrogen in the case of diolein). The equilibrium mixtures so formed were dissolved in light petroleum and cooled to precipitate the 1 : 3-diglyceride which was then removed by filtration. The filtrate was cooled further to precipitate the 1 : 2-diglycerides. The temperatures of crystallisation tabulated gave the best results.

	1 : 3-Diglyceride cryst. at	1 : 2-Diglyceride cryst. at	1 : 2-Diglyceride (yield, %)	1 : 3-Diglyceride (yield, %)
Distearin	35°	0°	40	58
Dipalmitin	35	0	44	55
Dimyristin	23	0	45	54
Dilaurin	23	0	44	55
Diolein	−20	(recovered from filtrate by evapn.)	47	47
Di-*p*-nitrobenzoate ...	20 (from $CHCl_3$)	—	—	—

The m. p. of the products are given in Table 1. 1 : 2-Diolein (I value 82·3; OH value 90·4) was further characterised by hydrogenation with palladium black to 1 : 2-distearin, m. p. 68·0° (OH value, 89·6).

Solubilities of Distearin Isomers in Light Petroleum.—Since the diglyceride isomers are separated surprisingly easily by crystallisation from light petroleum, it was of interest to determine their relative solubilities in this solvent. Saturated solutions of 1 : 2- and 1 : 3-distearin were kept overnight at 35°. Samples (5 ml.) of the clear supernatant solutions were then removed and evaporated and the residues dried to constant weight. 1 : 3-Distearin was found to have a solubility of 3·2 g./l. and 1 : 2-distearin had a solubility of 32 g./l.

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[*Received, September 24th,* 1958.]

[13] Howe and Malkin, *J.*, 1951, 2663.
[14] Malkin, Shurbagy, and Meara, *J.*, 1937, 1412.
[15] Daubert, Fricke, and Longenecker, *J. Amer. Chem. Soc.*, 1943, **65**, 2143.

153. *Constitutional Effects on the Hydrolysis of Amides in Concentrated Acid Solutions.*

By J. A. Leisten.

The rates of hydrolysis of 13 amides in 5·9, 7·2, and 8·5M-perchloric acid have been measured at 95°. The *A*2 mechanism is confirmed both by the observed steric effects, and by the polar effects which are treated quantitatively. The variation in rate with acid concentration is similar for the amides studied, but is not even approximately predicted by the Hammett–Zucker hypothesis.

Several features of the hydrolysis of amides in aqueous acids suggest the *A*2 mechanism: [1]

$$R{\cdot}CO{\cdot}NH_2 + H_3O^+ \overset{\text{Fast}}{\rightleftharpoons} R{\cdot}CO{\cdot}NH_3^+ + H_2O \quad \ldots\ldots\ldots (1)$$

$$R{\cdot}CO{\cdot}NH_3^+ + H_2O \xrightarrow{\text{Slow}} R{\cdot}CO_2H_2^+ + NH_3 \quad \ldots\ldots\ldots (2)$$

(The ammonia molecule then rapidly gains, and the carboxylic acidium ion rapidly loses, a proton. R may be an alkyl or an aryl group.) These features include constitutional effects in the amide molecule. Reid's experiments with substituted benzamides [2] show that the rate of hydrolysis in dilute acid, where equilibrium (1) lies to the left-hand side, is practically independent of polar influences in the molecule. It is clear from electronic principles that any change in the polar character of an amide would have opposite effects in steps (1) and (2) upon the overall rate of the reaction. Hence, in the absence of further knowledge Reid's results support, or at least accord with, the *A*2 mechanism. His results, however, require that the polar effects on steps (1) and (2) should be not only opposite, but nearly equal as well; and this leads to a more quantitative test of the mechanism with which the present work is concerned.

In principle, polar effects on step (2) can be separately examined by determining the

Table 1. *First-order rate constants for the hydrolysis of amides in aqueous perchloric acid solutions at* 95°.

Molarity of acid:	5·86	7·19	8·54
Acidity function, H_0:	−2·74	−3·75	−4·72
Amide *	k (hr.$^{-1}$)	k (hr.$^{-1}$)	k (hr.$^{-1}$)
p-Nitrobenzamide	—	1·40	0·53
m-Nitrobenzamide	1·92	1·10	0·44
m-Bromobenzamide	—	0·57	0·172
p-Bromobenzamide	—	0·39	—
Benzamide	0·64	0·228	0·073
m-Toluamide	—	0·188	0·057
p-Toluamide	0·37	0·129	—
p-tert.-Butylbenzamide	0·33	—	—
Anisamide	0·212	0·072	0·026
o-Bromobenzamide	—	0·099	—
o-Nitrobenzamide	—	0·040	—
o-Toluamide	—	0·027	—
Acetamide	2·27	0·88	0·332

* The amide concentration was 0·17M in each experiment.

rate of hydrolysis of differently substituted amides in a strongly acid solution, in which equilibrium (1) lies far to the right-hand side. Table 1 records the results of such measurements.

The results show that in strongly acid conditions polar effects are large, and in the

[1] (*a*) Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 785; (*b*) Bender, Ginger, and Kemp, *J. Amer. Chem. Soc.*, 1954, **76**, 3350; 1955, **77**, 348; (*c*) Edward and Meacock, *J.*, 1957, 2000.

[2] Reid, *Amer. Chem. J.*, 1899, **21**, 284; 1900, **24**, 397.

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direction to be expected if they were exerted only on the second step of the $A2$ mechanism: electron-attracting substituents accelerate the hydrolysis and electron-donating substituents retard it. In order to derive more quantitative conclusions we must consider the hydrolysis of *meta*- and *para*-benzamides in the dilute acid region where equilibrium (1) lies to the left. Let k_{ov} be the overall, *i.e.*, the observed, second-order rate constant, K_1 the equilibrium constant of the first step, and k_2 the first-order rate constant of the second step: the water concentration is not included in the kinetic equations since it is effectively constant in each experiment. The observed rate of the reaction $= k_{ov}$ [R·CO·NH$_2$][H$_3$O$^+$]. If we assume the $A2$ mechanism this rate also $= k_2$ [R·CO·NH$_3^+$] $= K_1k_2$ [R·CO·NH$_2$][H$_3$O$^+$].

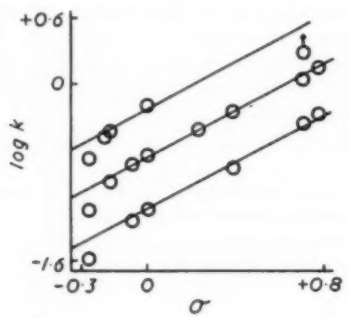
Therefore
$$k_{ov} = K_1k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The constants for benzamide itself being denoted by the suffix 0, it follows from (3) that

$$\left(\frac{k}{k_0}\right)_{ov} = \left(\frac{K}{K_0}\right)_1 \left(\frac{k}{k_0}\right)_2$$

and that
$$\log\left(\frac{k}{k_0}\right)_{ov} = \log\left(\frac{K}{K_0}\right)_1 + \log\left(\frac{k}{k_0}\right)_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

For side-chain reactions of *meta*- and *para*-benzene derivatives the Hammett equation, log k/k_0 (or log K/K_0) $= \sigma\rho$, applies generally.[3] σ is the substituent constant and ρ the reaction constant: ρ is a measure of the susceptibility of the reaction to polar substitution,



a positive value meaning that the rate or the equilibrium constant is increased by electron-attracting substituents. Applying the Hammett equation to (4), we have

$$\rho_{ov} = \rho_1 + \rho_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Now ρ_{ov}, determined from Reid's results, is +0·118;[3] and ρ_1, the reaction constant for the basic ionisation of amides, has been given the value −0·933.[1c] From equation (5) we can thus predict the value +1·05 for ρ_2. It being assumed for the present that equilibrium (1) lies far to the right in all the solutions studied, the rate constant in Table 1 may be identified with k_2, and the results used to determine ρ_2 directly. In the Figure, the logarithms of the rate constants are plotted against values of σ for each of the three perchloric acid solutions. The parallel straight lines are drawn with the calculated slope of +1·05. The slopes of the least-square plots give values of ρ_2, and these are listed below, with the number of results from which ρ_2 is determined (n), the standard deviation (s), and the correlation coefficient (r), for the two more concentrated solutions.[4] The agreement between the

[3] (*a*) Hammett, "Physical Organic Chemistry," McGraw-Hill, 1940, p. 184; (*b*) Jaffé, *Chem. Revs.*, 1953, **53**, 191.

[4] See ref. 3*b* for a discussion of s and r.

calculated and the determined values of ρ_2 is strong support, not merely for the *A*2 mechanism, but for the prevalence of this mechanism over the wide range of acidity from 0·5M-hydrochloric acid to 8·54M-perchloric acid.

$HClO_4$ (M)	ρ_2	n	s	r
7·19	1·12	8	0·071	0·989
8·54	1·19	6	0·055	0·995

It must now be considered that the reaction constants in equation (5) refer to the same temperature, whereas the value of ρ_1 was determined at 18°, that of ρ_2 at 95°, and that of ρ_{OT} at 100°. However, the reaction constant for the acid-catalysed hydrolysis of amides in aqueous alcohol, which corresponds to ρ_{OT}, has been shown to vary by only 0·26 over a 47° range of temperature,[5] and therefore the difference of 5° between the temperatures at which ρ_{OT} and ρ_2 have been obtained may be confidently disregarded. Moreover, pK_a values are in general insensitive to temperature:[6] still less sensitive will be a reaction constant calculated from pK_a values, for the temperature variations of the pK_a values will partially cancel in the calculation of the reaction constant. It is thus improbable that much error is introduced even by the large differences between the temperature at which ρ_1 and the other reaction constants were determined. It is noteworthy that the *A*2 mechanism already demands that equilibrium (1) should be insensitive to temperature. It can be shown that, in the dilute acid region where equation (5) holds, the observed activation energy is the sum of the standard enthalpy change in reaction (1) and the activation energy of step (2); whereas the latter alone is the observed activation energy in strongly acid solutions where k_2 is the observed rate constant. Thus, if the enthalpy change, which governs the temperature-dependence of equilibrium (1), is large, the observed activation energy should vary sharply in the region of acidity over which the position of the equilibrium moves from left to right. Such variations are not found.[7] Another assumption, already stated, is that the results in Table 1 all apply to systems in which equilibrium (1) lies far to the right-hand side. From the pK_a value for benzamide (−1·85 [1c]), the value for ρ_1 (−0·933), and the values of the acidity function for the three perchloric acid solutions,[8] it is possible to calculate the degree of conversion of the amides into their conjugate acids. The results are as follows. In the strongest (8·54M) solution, conversion into the conjugate acid is greater than 99% in all cases. In the 7·19M-solution the *least* basic amides, *m*- and *p*-nitrobenzamide, exist as conjugate acids to the extent of 95%. For these two solutions the assumption appears to be justified within experimental error. Even in the case of the weakest (5·86M) solution there is only one amide, *m*-nitrobenzamide, for which the proportion of conjugate acid, 65%, is so small as to produce an obvious error in the above calculations. This lone deviation can be observed in the Figure and is of the right magnitude for the explanation, a useful assurance that the present treatment is sound.

In dilute acid *ortho*-substituents in benzamide retard hydrolysis independently of their polar nature. The effect is clearly steric and according to present knowledge[9] it must operate on step (2), and not on step (1) which involves only a proton transfer. Similar effects should therefore be observable in the present work. The polar effects of substituents appear to be approximately similar in the *ortho*-position to those in the *para*-position.[10] Hence a rough estimate of steric retardation can be made by dividing the rate constant for an *ortho*-compound by that of the *para*-derivative. Some values of this ratio (k_{para}/k_{ortho}) are recorded below.

[5] Meloche and Laidler, *J. Amer. Chem. Soc.*, 1951, **73**, 1712.
[6] See, *e.g.*, Stokes and Robinson, "Electrolyte Solutions," Butterworths, 1955, p. 500, 505.
[7] Rabinowitch and Winkler, *Canad. J. Res.*, 1952, **20**, *B*, 73.
[8] Paul and Long, *Chem. Revs.*, 1957, **57**, 1.
[9] See, *e.g.*, Brown, *J.*, 1956, 1248.
[10] Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 3120.

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Substituent:	CH_3	Br	NO_2
Hydrolysis conditions		k_{para}/k_{ortho}	
0·5M-HCl, 100°	8	—	43
7·19M-$HClO_4$, 95°	5	4	35

The steric effects are clearly present in concentrated acid and of the same general magnitude as those in dilute acid, providing further evidence that the same, bimolecular, mechanism operates under both sets of conditions.

The variation in the rate of hydrolysis of the amides in solutions of different acidity may be predicted by means of the Hammett–Zucker hypothesis.[11] The observed rate of an *A*2 reaction is that of the second step, which for amide hydrolysis is $k_2[R{\cdot}CONH_3^+]$. To the approximation of the acidity-function concept, and under the conditions where the pre-equilibrium lies to the left-hand side, $[R{\cdot}CONH_3^+] \propto h_0$, and therefore the observed rate $\propto k_2h_0$. For such a reaction the Hammett–Zucker hypothesis predicts that the rate will be proportional to the acid concentration. Hence k_2 should be proportional to the acid

TABLE 2. *Calculated and observed variations of hydrolysis rate with acid concentration*

Hydrolysis conditions	k_2 in 5·86M-$HClO_4$ / k_2 in 7·19M-$HClO_4$		k_2 in 7·19M-$MClO_4$ / k_2 in 8·54M-$HClO_4$	
Amide	Obs.	Calc.	Obs.	Calc.
p-Nitrobenzamide	—	8·34	2·62	7·86
m-Nitrobenzamide	1·75	,,	2·51	,,
m-Bromobenzamide	—	,,	3·07	,,
Benzamide	2·82	,,	3·13	,,
m-Toluamide	—	,,	3·33	,,
p-Toluamide	2·87	,,	—	,,
Anisamide	2·93	,,	2·76	,,
Acetamide	2·57	,,	2·66	—
Average values	2·80 *	,,	2·87	7·86

* The low value for *m*-nitrobenzamide has been discounted as it arises from incomplete conversion into the conjugate acid.

concentration divided by h_0. In Table 2 the variation of k_2 calculated in this way from the Hammett–Zucker hypothesis is compared with that found directly.

The variations in rate are similar for the different amides; but the discrepancies between the observed and calculated values are large, and in the same direction as those found by Edward and Meacock for hydrolysis by sulphuric acid and hydrochloric acid.[1c] The calculated rates of hydrolysis in 8·54, 7·19, and 5·86M-acids are in the ratio 1 : 7·86 : 65·6. The experimental ratio, from the mean values at the bottom of Table 2, is 1 : 2·87 : 8·04. These results show a failure of the Hammett–Zucker hypothesis similar to that previously observed for aliphatic esters [13] and for ethylidene diacetate [14] in mineral acids of concentration greater than about 4M.

Experimental.—The amide specimens melted sharply in the ranges recorded in the literature. The solutions were prepared from " AnalaR " perchloric acid, and standardised against " AnalaR " benzoic acid. Benzamide and *m*-nitrobenzamide were hydrolysed in a flask from which samples were pipetted for analysis. Sealed tubes were used for the remaining amides which form sparingly soluble acids. Analysis was by the " formol " titration method.[13] Good first-order rate constants were obtained.

The author thanks Dr. A. E. Standage for amide specimens.

THE UNIVERSITY, SHEFFIELD. [*Received, September 25th,* 1958.]

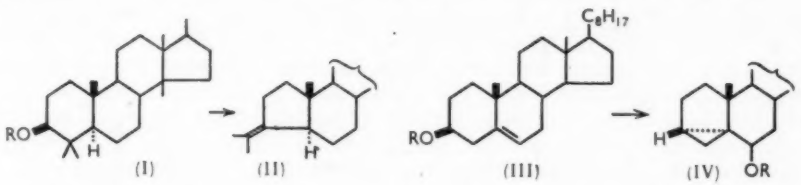
[11] Zucker and Hammett, *J. Amer. Chem. Soc.*, 1939, **61**, 2779; Long and Paul, *Chem. Revs.*, 1957, **57**, 935.
[13] Northrop, *J. Gen. Physiol.*, 1926, **9**, 767.
[13] Bell, Dowding, and Noble, *J.*, 1955, 3106.
[14] Bell and Lukianenko, *J.*, 1957, 1686.

154. *The Solvolysis of* 4 : 4-*Dimethylcholest-5-en-3β-yl Toluene-p-sulphonate.*

By Y. M. Y. Haddad and G. H. R. Summers.

Hydrolysis of 4 : 4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (V; R = *p*-$C_6H_4Me{\cdot}SO_2$) in aqueous acetone in the presence of potassium acetate yields 3-*iso*propylidene-A-norcholest-5-ene as major product, with 4 : 4-dimethylcholest-5-en-3β-ol and 4 : 4-dimethyl-3 : 5-*cyclo*cholestan-6β-ol as minor products. Acetolysis of (V; R = *p*-$C_6H_4Me{\cdot}SO_2$) and lanost-8 : 24-dien-3β-yl toluene-*p*-sulphonate also gives products of Wagner rearrangement and of substitution with retention of configuration. These solvolyses are considered to involve a unimolecular mechanism.

Two reactions, which have come to be considered as diagnostic of the presence of an equatorial 3-hydroxyl group in tetra- and penta-cyclic terpenoids, and Δ^5- steroids, involve rearrangement: dehydration (brought about by phosphorus pentachloride) of 3β-hydroxyterpenoids (I) causes Wagner rearrangement, with contraction of ring A and formation of *iso*propylidene-A-nor-derivatives [1] (II), and 3β-hydroxy-Δ^5-steroids [as the toluene-*p*-



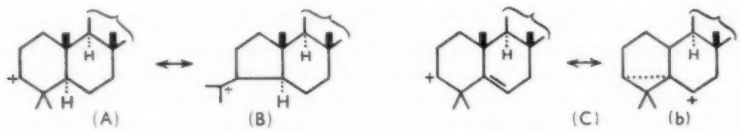
sulphonyl derivatives, R = *p*-$C_6H_4Me{\cdot}SO_2$ (III)] by solvolysis in buffered media yield 6β-substituted 3 : 5-*cyclo*steroids [2] (IV). The results contrast with the behaviour of the corresponding axial alcohols, which react principally by ionic 1 : 2-elimination without ring change.[3*] Wagner rearrangements depend upon ionisation,[5] and the alteration of the carbon skeleton by a 1 : 2-shift involves a carbonium ion. Thus the change (I ⟶ II) occurs by way of the cations (A, B), either as separate classical entities or as canonical structures of a non-classical mesomeric cation. The 3 : 5-*cyclo*steroid rearrangement is a 1 : 3-shift with stereospecific character which shows an accelerated rate (cf. cholestan-3β-yl toluene-*p*-sulphonate [6]); configurational,[7] kinetic,[8] and thermodynamic [9] studies lead to the conclusion that replacement reactions at position 3 of 3β-substituted Δ^5-steroids which lead to 1 : 3-rearrangement occur *via* a non-classical mesomeric ion (cf. C).

It was, therefore, of interest to examine structurally and kinetically the solvolysis of a system the geometry of which combined the configurational requirements of both the above rearrangements. For both rearrangements to occur concurrently, carbonium ion A

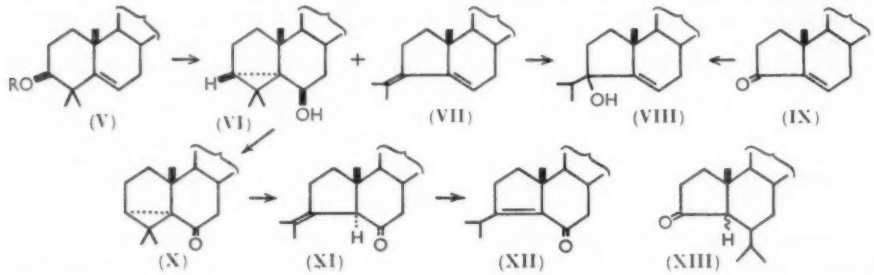
* Barton, Lewis, and McGhie [4] show that treatment of lanostan-3β-ol with phosphorus oxychloride in pyridine gives a mixture of lanost-2-ene and 3-*iso*propylidene-A-norlanostane.

[1] Dorée, McGhie, and Kurzer, *J.*, 1949, S 167; Ruzicka, Montavon, and Jeger, *Helv. Chim. Acta*, 1948, **31**, 818 (for lanosterol).
[2] Shoppee and Summers, *J.*, 1952, 3361, and references there cited.
[3] Barton, *Experientia*, 1950, **6**, 316; Evans and Shoppee, *J.*, 1953, 540.
[4] Barton, Lewis, and McGhie, *J.*, 1957, 2907.
[5] Meerwein and van Emster, *Ber.*, 1922, **55**, 2500.
[6] Nace, *J. Amer. Chem. Soc.*, 1952, **74**, 5937.
[7] Shoppee, *J.*, 1946, 1147.
[8] Winstein and Adams, *J. Amer. Chem. Soc.*, 1948, **70**, 838; Pearson, King, and Langer, *ibid.*, 1951, **73**, 414; Hafez, Halsey, and Wallis, *Science*, 1949, **110**, 475; Davies, Meecham, and Shoppee, *J.*, 1955, 679; Shoppee and Westcott, *J.*, 1955, 1891.
[9] Shoppee and Williams, *J.*, 1956, 2488; Simonetta and Winstein, *J. Amer. Chem. Soc.*, 1954, **76**, 18.

would become, in a modified form (introduction of a 5 : 6-double bond),* a canonical form of hybrid C. We now describe our structural investigations on the solvolysis of 4 : 4-dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (V; R = *p*-$C_6H_4Me{\cdot}SO_2$).



Hydrolysis of this ester (V; R = *p*-$C_6H_4Me{\cdot}SO_2$) in boiling aqueous acetone in the presence of potassium acetate for 14 hr. yielded 3β-hydroxy-4 : 4-dimethylcholest-5-ene (V; R = H) as a minor product (16%), an isomeric alcohol, m. p. 126°, $[\alpha]_D$ −25° (24%), and a hydrocarbon, m. p. 85°, $\lambda_{max.}$ 241 mμ (log ε 4·22) (60%). The hydrocarbon was also the major product of (*a*) acetolysis and (*b*) chromatography on basic aluminium oxide of the toluene-*p*-sulphonate [the minor and only other products were the acetate (V; R = Ac) and alcohol (V; R = H) respectively]. Since the amount of elimination accompanying



the 3 : 5-*cyclo*steroid rearrangement is normally small it was suspected that the hydrocarbon was 3-*iso*propylidene-A-norcholest-5-ene (VII), the product of rearrangement of the Δ^5-cation (C). Formation of 3 : 4-dimethylcholest-3 : 5-diene is excluded since the steric requirement of coplanarity of centres 3 and 4 and the 3β-ester and the 4β-methyl group is not satisfied. Structure (VII) was established by the formation of acetone on ozonolysis and by preparation of the compound from the ketone (IX) by treatment with *iso*propylmagnesium iodide. The last reaction gave also 3-*iso*propyl-A-norcholest-5-en-3α-ol (VIII) [which was dehydrated by phosphorus oxychloride in pyridine to the hydrocarbon (VII)], and a 5-membered ring ketone ($\nu_{max.}$ 1740 cm.$^{-1}$) [evidently 6-*iso*propyl-A-nor-5ξ-cholestan-3-one (XIV) formed by 1 : 4-addition of the Grignard reagent to the αβ-unsaturated ketone followed by ketonisation on hydrolysis].

The compound, m. p. 126°, we consider to be 4 : 4-dimethyl-3 : 5-*cyclo*cholestan-6β-ol (VI) from the evidence described below, its method of preparation, and the somewhat similar behaviour of the 6-hydroxyl group to that displayed by the secondary alcohol group in 6β-hydroxyoleanolic acid (sumaresinolic acid).[10] Its sensitivity to acids is shown by its conversion into the hydrocarbon (VII) by acetic acid and sulphuric or hydrochloric acid. It is notable that no 3β-substituted derivatives are produced by acid-catalysed rearrangement. Treatment with pyridine–acetic anhydride gave unchanged starting material, and sodium ethoxide at 180° (3 days) failed to yield an epimeric product.

Oxidation of the alcohol (VI) with chromium trioxide–pyridine gave a ketone in low yield, which showed carbonyl absorption at 1684 cm.$^{-1}$, consistently with conjugation

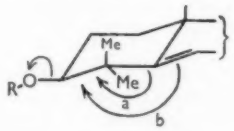
* The 5 : 6-double bond does not appreciably alter the geometry of ring A,[9] so that an equatorial bond at $C_{(3)}$ and the 4 : 5-linkage remain coplanar.

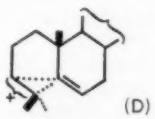
[10] Simonsen and Ross, " The Terpenes," Cambridge Univ. Press, 1957, Vol. V, p. 302.

between the *cyclo*propane and the carbonyl group and formulation of the product as 4 : 4-dimethyl-3 : 5-*cyclo*cholestan-6-one (X). The alcohol (VI) was not oxidised by aluminium *tert.*-butoxide; chromium trioxide in acetic acid gave some of the hydrocarbon (VII) and a crystalline product in small yield, which was shown by the strong absorption bands at 1733, 1684, and 1242 cm.$^{-1}$ to be a mixture of the ketone (X) and 3β-acetoxy-4 : 4-dimethylcholest-5-ene (V; R = Ac). Acid-isomerisation of the ketone (X) gave an oil, $\lambda_{max.}$ 259 mμ (log ε, 4·0), which on account of its ultraviolet absorption is thought to be 3-*iso*propyl-A-norcholest-3-en-6-one (XII) formed *via* (XI).

Position 6 in oleanane derivatives has been well established as the most hindered position in the molecule: *e.g.*, sumaresinolic acid yields the 3-monoacetate,[11] and the 6-ketone (readily formed on oxidation of the 3β-monoacetate with chromium trioxide in pyridine) resists reduction by both the Clemmensen and the Wolff–Kishner method * [11] although the modified procedure of the latter method has more recently been shown to give 33% of the deoxo-compound.[12] It seems that the lower reactivity of the alcohol (VI) than of 6β-hydroxyoleanolic acid can be tentatively related to a significant but, at present, indeterminable hindrance on the α-side of the molecule due to distortion of ring A by the 3 : 5-transannular bond (cf. the reactions of 6-keto-3 : 5-*cyclo*steroids with lithium aluminium hydride [13] and Grignard reagents [14] which give the 3 : 5-*cyclo*-6α-alcohols).

The above solvolyses agree in the main with the general pattern [4] for substitution of 3β-substituted Δ^5-steroids by weak nucleophiles.[8] Thus, in an acidic medium retention of configuration with little or no elimination occurs, whilst in a buffered medium rearrangement is the normal reaction. The significant difference is that Wagner rearrangement is predominant in both media, indicating that the easier reaction is the cleavage of the 4 : 5-bond with attack at position 3 with inversion. This is to be expected if one considers that 3β-substituted 4 : 4-dimethyl-steroids and -terpenes contain an α-substituted *neo*-pentyl system which is especially prone to rearrangement.[15] The steric conditions necessary for the formation of the above products are also suitable, the overall interaction at position 3 involving (a) α-stereoelectronic competition of the σ-electrons of the 4 : 5-bond and (b) the π-electrons of the 5 : 6 double bond. As has been previously pointed out, process (b) is known to lead to the mesomeric cation C, but for process (a) no information is




(D)

yet available, for the example cited, about the nature of the resulting cation or cations. To test whether in fact a charge produced at position 3 by heterolysis completely migrates to position 4, giving cation B, we examined the acetolysis of lanosta-8 : 24-dien-3β-yl toluene-*p*-sulphonate. Treatment with potassium acetate in acetic acid at 90° for 3 hr. gave predominantly the *iso*propylidene derivative and a little lanosta-8 : 24-dien-3β-yl acetate. There was no evidence of inversion without rearrangement, a result indicating an ionic mechanism and contrasting with the accepted behaviour of nucleophilic substitution at position 3 in saturated steroids.[16] The accompanying retention of configuration

* The 6-keto-group is not reduced by sodium borohydride.[12]

[11] Ruzicka, Jeger, Grob, and Hosli, *Helv. Chim. Acta*, 1943, **26**, 2283.
[12] Djerassi, Thomas, and Jeger, *Helv. Chim. Acta*, 1955, **38**, 1304.
[13] Ref. 2; cf. Wagner and Wallis, *J. Amer. Chem. Soc.*, 1950, **72**, 1047; Wagner, Wolff, and Wallis, *J. Org. Chem.*, 1952, **17**, 529.
[14] Summers, unpublished work.
[15] Ingold, *J.*, 1953, 2845.
[16] Shoppee, *J.*, 1946, 1138; Bridgewater and Shoppee, *J.*, 1953, 1709.

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suggests the intermediate existence either of carbonium ions A and B (the latter more stable) as separate entities, or of a bridged carbonium ion D in which the charge is distributed over carbon atoms 3 and 4. A decision between these two possibilities would depend upon whether the rate of solvolysis was normal or accelerated (anchimeric assistance) as compared with, say, that for pinacolyl toluene-*p*-sulphonate. Stabilisation of the distributed positive charge by the π-orbital of the 5 : 6-double bond (b) could then lead to the 6β-3 : 5-*cyclo*-derivative by interaction of an anion at the electron-deficient centre 6. The non-classical mesomeric ion C would consequently have to be modified to a structure involving resonance between bridged ion D and canonical form C (b) (cf. the stabilisation of " phenonium " ions by resonance [9]).

Experimental

Ultraviolet absorption spectra were determined for ethanol solutions in a Unicam S.P. 500 spectrophotometer. Infrared absorption spectra were measured by use of a Grubb-Parsons GS2 double-beam grating spectrometer. Unless otherwise stated, alumina used was Spence's type H (activity II). $[\alpha]_D$ refer to chloroform solutions.

4 : 4-*Dimethylcholest-5-en-3β-yl Toluene*-p-*sulphonate*.—**4 : 4**-Dimethylcholest-5-en-3β-ol (5 g.) in pyridine (40 ml.) was treated with toluene-*p*-sulphonyl chloride (5 g.) and left overnight. Working up in the usual way gave an oil (7·3 g.) which on crystallisation from pentane gave **4 : 4-*dimethylcholest-5-en-3β-yl toluene*-p-*sulphonate*** as needles, m. p. 92—95° (decomp.), $[\alpha]_D$ −46°, −45° (*c* 0·88, 1·4) [Found (after drying at 25°/0·02 mm. for 16 hr.): C, 76·3; H, 9·75. $C_{36}H_{56}O_3S$ requires C, 76·01; H, 9·9%].

3 : 5-cyclo-4 : 4-*Dimethylcholestan*-6β-*ol*.—A solution of **4 : 4**-dimethylcholest-**5**-**en**-**3β**-yl toluene-*p*-sulphonate (11 g.) in acetone (240 ml.) was treated with water (60 ml.) and anhydrous potassium acetate (10 g.) and refluxed for 14 hr. The acetone was removed by evaporation under reduced pressure and the product extracted with ether. The ethereal extract was washed with water, dried (Na_2SO_4), and evaporated, giving an oil which was chromatographed on aluminium oxide (170 g.). Elution with hexane (2 × 200 ml.) gave an oil (6·23 g.) which on crystallisation from ethyl acetate gave **3-iso*propylidene*-A-*norcholest-5-ene***, m. p. 85°, $[\alpha]_D$ −65·7° (*c* 1·4), $\lambda_{max.}$ 241 mμ (log ε 4·22) [Found (after drying at 25°/0·02 mm. for 16 hr.): C, 87·5; H, 12·6. $C_{28}H_{48}$ requires C, 87·8; H, 12·2%]. This compound gave a positive Rosenheim test. Elution with benzene–ether (4 : 1) (7 × 200 ml.) gave a solid (2·66 g.) which on crystallisation from acetone gave **3 : 5-cyclo-4 : 4-*dimethylcholestan*-6β-*ol*** as plates, m. p. 125—126°, $[\alpha]_D$ −24·7° (*c* 0·9) [Found (after drying at 40°/0·02 mm. for 18 hr.): C, 83·4; H, 12·0. $C_{28}H_{50}O$ requires C, 84·0; H, 12·15%]. Repeated elution with chloroform gave a solid (1·18 g.) which on crystallisation from acetone gave **4 : 4**-dimethylcholest-5-en-3β-ol, m. p. 146—148°, $[\alpha]_D$ −61·6° (*c* 0·9).

Treatment of **4 : 4**-dimethyl-**3 : 5-*cyclo*cholestan**-6β-ol with pyridine–acetic anhydride for 1 month failed to bring about acetylation, and starting material was recovered quantitatively.

3-iso*Propylidene*-A-*norcholest-5-ene*.—(*a*) **4 : 4**-Dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (433 mg.) in pentane (5 ml.) was added to a column of aluminium oxide (15 g.) in pentane and left for 1 hr. Elution with pentane (3 × 30 ml.) gave an oil (240 mg.) which on crystallisation from ethyl acetate–methanol gave **3-*iso*propylidene-A-norcholest-5-ene**, m. p. and mixed m. p. 80—82°. Elution with ether and chloroform gave **4 : 4**-dimethylcholest-5-en-3β-ol, m. p. 147—149°.

(*b*) **4 : 4**-Dimethylcholest-5-en-3β-ol (426 mg.) in hexane (50 ml.) was shaken for 0·5 hr. with phosphorus pentachloride (500 mg.). Filtration of the solution through aluminium oxide gave an oil which by repeated crystallisation from ethyl acetate gave **3-*iso*propylidene-A-norcholest-5-ene**, m. p. 80—83°.

(*c*) **4 : 4**-Dimethyl-**3 : 5-*cyclo*cholestan**-6β-ol (60 mg.) in acetic acid (5 ml.) was treated with hydrochloric (or sulphuric) acid (4 drops) and left for 0·5 hr. Working up in the usual way gave **3-*iso*propylidene-A-norcholest-5-ene**, m. p. 81—82° (from ethyl acetate at 0°).

(*d*) A-Norcholest-5-en-3-one (1·1 g.; m. p. 96°) in ether (50 ml.) was added to an ether solution of *iso*propylmagnesium iodide, prepared from magnesium (1 g.) and *iso*propyl iodide (3·6 ml.), and refluxed for 2·5 hr. The solution was poured into ice and ammonium chloride solution and extracted with more ether, and the ethereal extract washed with water, dried, and evaporated, to give an oil (1·07 g.) which was chromatographed on neutral aluminium oxide

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(40 g.; Woelm). Elution with pentane gave an oil (71 mg.) whose infrared spectrum was that of 3-*iso*propylidene-A-norcholest-5-ene prepared as above. Elution with hexane (8 × 200 ml.) gave 6-iso*propyl-A-nor-5ξ-cholestan-3-one* (760 mg.), m. p. 225—227° (from ethyl acetate), $[\alpha]_D$ +94°, +90·3° (*c* 1·4, 0·8) $\lambda_{max.}$ CCl_4 1740 cm.$^{-1}$ [Found (after drying at 40°/0·02 mm. for 18 hr.): C, 83·5; H, 11·8. $C_{29}H_{50}O$ requires C, 84·0; H, 12·15%]. Elution with ether gave a semisolid material (270 mg.) which was rechromatographed on neutral aluminium oxide (7 g.). Elution with benzene gave 6-*iso*propyl-A-nor-5ξ-cholestan-3-one, m. p. 225—228° (132 mg.); then elution with ether gave an oil (135 mg.) which was dehydrated by phosphorus oxychloride in pyridine at 0°. The oil so obtained crystallised with difficulty from ethyl acetate–methanol; the product had m. p. and mixed m. p. 78—83°.

Ozonolysis of 3-iso*Propylidene-A-norcholest-5-ene.*—3-*iso*Propylidene-A-norcholest-5-ene (1·76 g.) in carbon tetrachloride (100 ml.) was treated with excess of ozone at 0° for 2 hr. The solvent was evaporated under reduced pressure and the resulting oil boiled for 1 hr. with water (120 ml.). The aqueous mixture was distilled and the distillate treated with dinitrophenylhydrazine sulphate solution and left at 0° overnight. The orange solid was collected and crystallised from aqueous methanol, to give needles of acetone phenylhydrazone, m. p. and mixed m. p. 124—125°.

Attempted Epimerisation of 4 : 4-*Dimethyl*-3 : 5-cyclo*cholestan*-6β-*ol.*—4 : 4-Dimethyl-3 : 5-*cyclo*cholestan-6β-ol (500 mg.) was heated with sodium (1 g.) and ethanol (10 ml.) at 190° for 75 hr. After cooling, the solid was treated with water and extracted with ether. The ethereal extract was washed with water, dried, and evaporated to give an oil which readily crystallised (m. p. 117—126°). Careful chromatography on basic alumina (Woelm) failed to yield an epimeric product, and starting material (466 mg.) was recovered.

4 : 4-*Dimethyl*-3 : 5-cyclo*cholestan*-6-*one.*—4 : 4-Dimethyl-3 : 5-*cyclo*cholestan-6β-ol (3·5 g.) in pyridine (35 ml.) was treated with chromium trioxide (3·5 g.) and pyridine (35 ml.), and left overnight. The solution was diluted with ether and filtered, and the solvent evaporated under reduced pressure. The sticky solid obtained was chromatographed on aluminium oxide (90 g.). Elution with benzene–pentane (1 : 1) gave oils (310 mg.) which by repeated crystallisation from acetone–methanol gave 4 : 4-*dimethyl*-3 : 5-cyclo*cholestan*-6-*one*, m. p. 96—98°, $[\alpha]_D$ +83° (*c* 0·9), $\lambda_{max.}$ 1684 cm.$^{-1}$ in carbon tetrachloride [Found (after drying at 20°/0·02 mm. for 10 hr.): C, 84·0; H, 11·5. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%]. Elution with benzene, ether, and chloroform gave starting material (2·85 g.), m. p. 123—126°, $[\alpha]_D$ −21° (*c* 1·0).

The ketone (120 mg.) in acetic acid (10 ml.) containing 5N-sulphuric acid (2·5 ml.) was refluxed for 2 hr. Isolation of the product in the usual way gave an oil (87 mg.), $\lambda_{max.}$ 259 mμ (log ε 4·0).

Acetolysis of 4 : 4-*Dimethylcholest-5-en-3β-yl Toluene*-p-*sulphonate.*—4 : 4-Dimethylcholest-5-en-3β-yl toluene-*p*-sulphonate (890 mg.) in acetic acid (40 ml.) containing anhydrous potassium acetate (8 g.) was heated at 95° for 3 hr. The product after isolation in ether was hydrolysed with 5% methanolic potassium hydroxide (40 ml.), and the resulting oil chromatographed on aluminium oxide (24 g.). Elution with pentane (2 × 100 ml.) gave 3-*iso*propylidene-A-norcholest-5-ene (448 mg.), m. p. 79—81° (from ethyl acetate–methanol), $[\alpha]_D$ −64° (*c* 2·0). Elution with chloroform gave solid 4 : 4-dimethylcholest-5-en-3β-ol (198 mg.), needles (from acetone), m. p. 141—144°, $[\alpha]_D$ −61° (*c* 0·7).

Lanosta-8 : 24-*dien*-3β-*yl Toluene*-p-*sulphonate.*—Lanosta-8 : 24-dien-3β-ol (3·5 g.) in pyridine (30 ml.) was treated at 0° with toluene-*p*-sulphonyl chloride (3 g.) and left overnight. The product, an oil (4·7 g.), crystallised from ethyl acetate as needles, m. p. 116—122°. Recrystallisation from pentane at 0° gave *lanosta*-8 : 24-*dien*-3β-*yl toluene*-p-*sulphonate*, m. p. 119—124°, $[\alpha]_D$ +42·6° (*c* 0·9) [Found (after drying at 40°/0·02 mm. for 18 hr.): C, 76·3; H, 50·0. $C_{37}H_{56}O_3S$ requires C, 76·5; H, 9·7%].

Acetolysis of Lanosta-8 : 24-*dien*-3β-*yl Toluene*-p-*sulphonate.*—Lanosta-8 : 24-dien-3β-yl toluene-*p*-sulphonate (2·06 g.) in acetic acid (40 ml.) containing anhydrous potassium acetate (2 g.) was heated at 95° for 3 hr. The product, an oil, was hydrolysed by refluxing 5% methanolic potassium hydroxide (40 ml.) for 1 hr. The resulting solid was chromatographed on aluminium oxide (40 g.). Elution with pentane (2 × 200 ml.) gave 3-iso*propylidene-A-norlanosta*-8 : 24-*diene* (1·21 g.), m. p. 134—136° (from ethyl acetate), $[\alpha]_D$ +81° (*c* 0·9). Elution with ether and chloroform gave lanosterol (291 mg.), m. p. 138—139° (from ether–methanol), $[\alpha]_D$ +56°, +54° (*c* 1·1, 1·2). The infrared spectrum was identical with that of a pure specimen of lanosterol.

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3-iso*Propylidene*-A-*norlanosta*-8 : 24-*diene*.—Lanosterol (995 mg.) in hexane (100 ml.) was shaken with phosphorus pentachloride (1 g.) for 0·5 hr., then added to a column of aluminium oxide (20 g.) in hexane and eluted with hexane, to give 3-*iso*propylidene-A-norlanosta-8 : 24-diene, m. p. 138—140° (from acetone), $[\alpha]_D$ +82° (*c* 0·9) [Found (after drying at 40°/0·02 mm. for 18 hr.): C, 88·2; H, 11·9. Calc. for $C_{30}H_{48}$: C, 88·2; H, 11·8%].

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155. *The Composition of the Alkali-stable Polysaccharide of Sugar-beet Pectin.*

By P. ANDREWS, L. HOUGH, D. B. POWELL, and B. M. WOODS.

The polysaccharide isolated by extracting sugar-beet chips with hot lime-water was found to contain L-arabinose, D-galactose, L-rhamnose, and galacturonic acid, in the approximate proportions of 74, 10, 3·5, and 5% respectively, and smaller quantities of 2-*O*-methyl-D-xylose, 2-*O*-methyl-L-fucose, mannose, fucose, and an aldobiouronic acid composed of galacturonic acid and 2-*O*-methylxylose. The polysaccharide preparation had an average molecular weight of about 12,500 and attempts to fractionate the material were unsuccessful. It is suggested therefore that the "araban" component of pectin exists in combination with a variety of monosaccharide units.

THE pectic polysaccharides exist in such close physical union that very few cases are recorded of a pectin component isolated in a pure state. Material is usually carefully selected so that a pectin rich in one particular component can be utilised, but even so chemical treatment is generally necessary to remove the other components. For example, it has been shown that sugar-beet pectin can be degraded with lime-water to an alkali-stable polysaccharide consisting in the main of L-arabinose units.[1] A further study of this material has now revealed new details of its fine structure.

Sugar-beet chips were extracted with hot lime-water to give a 5% yield of the alkali-stable polysaccharide which was unaffected by further heating in saturated lime-water at 80° for 24 hr. Hydrolysis of this material with N-sulphuric acid followed by passage of the hydrolysate through an anion-exchange resin afforded a mixture of neutral sugars, which was fractionated on a cellulose column.[2] L-Arabinose, D-galactose, and L-rhamnose were isolated and characterised; traces of mannose were also revealed. A small uronic acid fraction, which from its behaviour on paper chromatograms seemed to consist largely of aldobiouronic acids, was displaced from the resin column by sulphuric acid. Vigorous hydrolysis of this fraction followed by paper chromatography suggested the presence of galactose, arabinose, rhamnose, and hexuronic acid. After prior treatment with methanolic hydrogen chloride the uronic acids were reduced with borohydride,[3] and subsequent hydrolysis and paper chromatography revealed the same neutral components as before, but with an increased proportion of galactose. This observation, coupled with the absence of glucurono-6 ⟶ 3-lactone, led to the conclusion that galacturonic acid was present in the polysaccharide and that it was linked glycosidically to galactose, arabinose, and rhamnose. Quantitative analysis of the polysaccharide indicated the presence of L-arabinose, D-galactose, L-rhamnose, and galacturonic acid in the approximate molecular proportions of 21 : 3 : 1 : 1·5.

Electrophoresis[4] of the polysaccharide in three buffers of pH 7·0, 8·0, and 5·2 respectively gave peaks which migrated towards the anode, presumably because of the hexuronic

[1] Scheilber, *Ber.*, 1873, **6**, 612; Hirst and Jones, *J.*, 1948, 2311.
[2] Hough, Jones, and Wadman, *J.*, 1949, 2511; 1950, 1702.
[3] Jones and Reid, *Canad. J. Chem.*, 1955, **33**, 1682.
[4] Colvin, Cook, and Adams, *Canad. J. Chem.*, 1952, **30**, 603; Speizer, Copley, and Nutting, *J. Phys. Colloid Chem.*, 1947, **51**, 117; Lindquist, *Biochem. Biophys. Acta*, 1953, **10**, 580; Northcote, *Biochem. J.*, 1954, **58**, 353; Record and Grinstead, *ibid.*, 1953, **53**, 671.

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acid constituents. A single peak was observed in each buffer, although in the acetate buffer (pH 5·2) the peak became rather diffuse. However, on reversal of the current, a single compact peak was again formed. The latter result is compatible with heterogeneity due to slight differences in the molecular constitution of the polysaccharide molecules rather than to a mixture of quite different molecular species such as araban and polygalacturonic acid, which would probably be resolved on electrophoresis into two distinct components. Attempts to fractionate the polysaccharide, and so obtain a polysaccharide further enriched in arabinose, by copper-complex formation, alcohol–water extraction, and Cetavlon precipitation were all unsuccessful.

Acetylation of the sugar-beet polysaccharide with acetic anhydride in pyridine gave an acetate ($[\alpha]_D$ −87° in $CHCl_3$) which was fractionated with chloroform–light petroleum into four main fractions (see Table 1). Each fraction was deacetylated and hydrolysed. Examination on paper chromatograms revealed little difference in composition; rhamnose and galactose were still present in each fraction, and traces of uronic acid were also apparent. Determination of the average molecular weight of the largest fraction of the acetylated polysaccharide by an isopiestic method [5] gave a value of 20,550 which corresponds to 12,500 for the free polysaccharide. Values of 6300 and 10,000 have been reported for araban fractions of sugar beet by Gaponekov [6] and Ingleman [7] respectively. Application of the acetic acid–trifluoracetic anhydride reagent [8] to the acetylation of the sugar-beet polysaccharide caused considerable degradation, loss of arabinose units being indicated by the optical rotation of the polysaccharide acetate ($[\alpha]_D$ −12° in $CHCl_3$). Hydrolysis of the deacetylated polysaccharide verified this conclusion since on paper chromatograms greatly increased proportions of rhamnose, galactose, and uronic acid, relative to the arabinose, were found.

In a partial hydrolysis experiment designed for the isolation of oligosaccharides, a polysaccharide solution was adjusted to pH 2·0 with sulphuric acid and heated at 80°. The products were fractionated on a charcoal column,[9] with water–alcohol for elution. Galactose and arabinose, rhamnose and fucose, two mono-*O*-methyl sugars, and oligosaccharides appeared in successive fractions from the column. The mono-*O*-methyl sugars were obtained crystalline, after separation on paper chromatograms, and were identified as 2-*O*-methyl-D-xylose and 2-*O*-methyl-L-fucose. Another compound, also isolated in small amount, appeared to be an aldobiouronic acid composed of galacturonic acid and 2-*O*-methylxylose.

The detection of these mono-*O*-methyl sugars in the polysaccharides of plum leaves [10] and in sugar-beet and sisal pectin [11] with the aid of charcoal adsorption and desorption suggests that they are normal constituents of pectin but hitherto have escaped detection because of the small quantities present.

Experimental

Partition chromatography by the descending method was carried out on Whatman No. 1 filter paper, with one of the following solvent systems: (*a*) ethyl acetate–acetic acid–water (9 : 2 : 2 v/v); (*b*) butan-1-ol–pyridine–water (10 : 3 : 3 v/v); (*c*) butan-1-ol–ethanol–water (40 : 11 : 19 v/v). Sugars were detected on the chromatograms with *p*-anisidine hydrochloride.[3] Amberlite ion-exchange resins were used throughout. Unless otherwise stated, optical rotations were determined for aqueous solutions at 25°.

Preparation of the Alkali-stable Polysaccharide.—Sugar beet in the form of dry chips was kindly provided by Dr. A. Carruthers of the British Sugar Corporation. In their preparation,

[5] Barger, *J.*, 1904, 286; Barker and Bourne, *J.*, 1952, 209.
[6] Gaponekov, *J. Gen. Chem.* (*U.S.S.R.*), 1937, **7**, 1729; *Chem. Abs.*, 1937, **31**, 8307.
[7] Ingleman, *Comm. Swed. Sugar Corp.*, 1945, **1**, 179; *Chem. Abs.*, 1945, **39**, 5525.
[8] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976.
[9] Andrews, Hough, and Powell, *Chem. and Ind.*, 1956, 658.
[10] Andrews and Hough, *J.*, 1958, 4476.
[11] Aspinall and Cañas-Rodriguez, *J.*, 1958, 4020.

sugar-beet slices had been thoroughly extracted with water at *ca.* 70° to remove sucrose and other soluble materials, then the residual material was pressed and air-dried.

The chips (1·8 kg.) were heated with saturated lime-water (18 l.) at 60—65° for 16 hr., during which sodium hydrogen sulphite (*ca.* 5 g.) was stirred into the mixture in order to reduce the formation of dark products. After the slurry had cooled, as much liquid as possible was extracted from it by use of a press. The extract was then filtered through a Nylon stocking and finally clarified by passage through a Sharples high-speed centrifuge. The resultant solution (13 l.) was acidified with acetic acid, and methylated spirits (52 l.) added to precipitate the polysaccharide. This precipitate was dissolved in the minimum volume of water, and the solution, after clarification on the centrifuge, dialysed against tap-water for 1 week. Adding ethanol (4 vol.) to the dialysed solution precipitated the crude polysaccharide, which was isolated on the centrifuge, washed with ethanol and ether, and dried over phosphoric oxide (yield, 100 g.). This material had $[\alpha]_D$ −84° (*c* 1·0) (Found: N, 0·8; sulphated ash, 5·1%).

For quantitative studies, this product was further purified by passage of a 1% solution through a column of mixed IR-120(H) and IR-4B(OH) resins (1 : 3 w/w), the efficiency of the de-ionisation process being checked by measuring the conductivity of the column effluent. The polysaccharide was reprecipitated with ethanol, collected on the centrifuge, washed with ethanol and ether, and dried; this material had $[\alpha]_D$ −108° ± 3° (*c* 1·0) (Found: N, 0·8; OMe, 0·8; sulphated ash, 0·9%). The supernatant liquid was concentrated, and the small residue examined on paper chromatograms. The presence of a trace of arabinose was detected.

Electrophoresis of the Polysaccharide.—Solutions of the purified polysaccharide (1·25% w/v) in 0·05M-phosphate buffer (pH 7·0), 0·20M-borate buffer (pH 8·0), and 0·1M-acetate buffer (pH 5·2) were clarified on the high-speed centrifuge. The supernatant liquors were dialysed against the appropriate buffer (1 l.) for 24 hr. at 4°. After the conductivities of the resultant solutions had been checked, electrophoresis was carried out in a Tiselius apparatus at 4°, with a potential of 320—420 v and a current of 15—18 m. amps. Photographs of the migrating boundaries were taken at various times up to 5 hr., after which the boundaries became diffuse.

Preparation of the Acetylated Polysaccharide.—(a) *With acetic anhydride.* The crude polysaccharide (13 g.) was suspended in dry pyridine (650 c.c.), and acetic anhydride (200 c.c.) was added during several hours with stirring. The mixture was then heated at 95—100° for 6 hr., then cooled, and insoluble material was removed on the centrifuge. The supernatant liquid was poured into water, and the precipitate of crude acetylated polysaccharide collected, washed with water, and reprecipitated from acetone solution. The final product (6·7 g.) had $[\alpha]_D$ −87° ± 2° (*c* 0·8 in $CHCl_3$) (Found: Ac, 38·5. Calc. for di-*O*-acetylpentan: Ac, 39·8%).

The acetylated polysaccharide (5 g.) was fractionated by heating it under reflux with mixtures of chloroform and light petroleum (b. p. 40—60°); each extraction was for 0·5 hr. with 100 c.c. of solvent mixture. Each of the four fractions so obtained (see Table 1) was dissolved in ice-cold chloroform, and deacetylated with sodium methoxide as described by Hirst, Percival, and Wylam.[12] The regenerated polysaccharide was purified by precipitation from aqueous solution with methanol, then washed with methanol and ether, and dried over phosphoric oxide.

TABLE 1. *Fractionation of acetylated polysaccharide.*

	Acetylated polysaccharide			
Fraction	$CHCl_3$–light petroleum (v/v)	Yield (g.)	$[\alpha]_D$ (in $CHCl_3$)	Deacetylated product, $[\alpha]_D$ (in H_2O)
1	35 : 65	0·05	−61° ± 5° (*c* 0·9)	Insol. in water
2	40 : 60	0·16	−118 ± 7 (*c* 0·3)	−104 ± 8° (*c* 0·4)
3	45 : 55	0·30	−102 ± 2 (*c* 0·8)	−100 ± 5 (*c* 0·3)
4	50 : 50	4·31	−84 ± 2 (*c* 1·2)	−95 ± 2 (*c* 1·1)

(b) *With trifluoracetic anhydride.*[8] Trifluoracetic anhydride (16·5 c.c.) was added dropwise to a suspension of polysaccharide (1 g.) in glacial acetic acid (15 c.c.). The mixture was stirred for 4 hr. at 20°, then poured into water. The acetylated material which separated was collected, washed with water, and dissolved in chloroform. After being dried (K_2CO_3), the chloroform solution was evaporated to a crisp brown solid (0·56 g.) with $[\alpha]_D$ −11·5° ± 1·5° (*c* 1·4 in $CHCl_3$) (Found: Ac, 37·9%). Deacetylation in chloroform solution with sodium methoxide gave a water-soluble product with $[\alpha]_D$ +27° ± 2° (*c* 0·8).

[12] Hirst, Percival, and Wylam, *J.*, 1954, 189.

Qualitative Analysis of the Alkali-stable Polysaccharide.—Samples of the crude and purified polysaccharides were hydrolysed in N-sulphuric acid at 100° for 16 hr. After neutralisation with barium carbonate and evaporation, the hydrolysates were examined on paper chromatograms. The presence in each of a large quantity of arabinose and minor quantities of galactose, rhamnose, and hexuronic acid was revealed. A sample of the alkali-stable polysaccharide prepared previously by Hirst and Jones [1] was similarly hydrolysed, and appeared to have a similar composition. The polysaccharide regenerated from fractions **2**, **3**, and **4** of the acetylated material (see Table 1) also contained galactose and rhamnose in addition to large amounts of arabinose, and traces of hexuronic acid. In contrast, the polysaccharide regenerated from the material acetylated with trifluoracetic anhydride as catalyst contained much greater proportions of galactose, rhamnose, and hexuronic acid, relative to the arabinose.

For characterisation of the above constituents, the alkali-stable polysaccharide (3 g.) was hydrolysed in N-sulphuric acid (50 c.c.) at 100° for 20 hr. The cooled hydrolysate was passed through a column of IR-4B(OH) resin, and the neutral effluent concentrated, yielding a syrup (2·1 g.) which was fractionated by partition chromatography on a cellulose column (25 × 4 cm.), with butan-1-ol, half-saturated with water, as the mobile phase. The following monosaccharides and derivatives were obtained: L-Arabinose (1·3 g.), m. p. and mixed m. p. 151°, $[\alpha]_D$ +103° (equil.; *c* 1·0); *N*-benzoylhydrazone, m. p. and mixed m. p. 187°. D-Galactose (150 mg.), m. p. 157°, mixed m. p. 158°, $[\alpha]_D$ +77° (equil.; *c* 0·6). L-Rhamnose (40 mg.), $[\alpha]_D$ +11° (measured on solution of anhydrous syrup; *c* 0·3); *N*-benzoylhydrazone, m. p. and mixed m. p. 179°. A compound (*ca.* 5 mg.) which co-chromatographed with mannose was also isolated.

Examination of the Acidic Components of the Alkali-stable Polysaccharide.—The acidic carbohydrates retained on the IR-4B resin column, through which the polysaccharide hydrolysate had been passed (see above), were displaced from it by elution with N-sulphuric acid. The effluent was neutralised with barium carbonate, and the solution filtered and evaporated to dryness. The residue (0·3 g.) was extracted several times with hot methanol to remove any neutral sugars, then dissolved in water, and the solution was passed through a column of IR-120(H) resin. The acidic solution so obtained was evaporated at 30°, and yielded a syrup (0·21 g.) which was shown by paper chromatography to contain hexuronic acid and acidic oligosaccharides, but glucurono-6 ⟶ 3-lactone was not detected. A portion (30 mg.) of the syrup was heated in 2N-sulphuric acid at 100° for 16 hr., and the products were examined on the paper chromatogram; galactose, rhamnose (ratio roughly 1 : 1, estimated visually), hexuronic acid, and a trace of arabinose were observed.

The remainder of the syrup (180 mg.) was heated under reflux with methanol containing hydrogen chloride (4% w/w) for 16 hr. The solution was then neutralised with silver carbonate, filtered, and concentrated, and the residue dissolved in 0·1M-sodium borohydride (10 c.c.). After 3 hr., excess of borohydride was decomposed by addition of dilute acetic acid, and the solution passed through columns of IR-120(H) and IR-4B(OH) resins. The effluent was concentrated to dryness, and the residue hydrolysed by N-sulphuric acid for 16 hr. at 100°. Paper chromatography of the hydrolysate indicated the presence of galactose, rhamnose (ratio roughly 3 : 1), and arabinose; glucose was not detected.

Isolation of Other Monosaccharide Components of the Alkali-stable Polysaccharide.—As a preliminary to the isolation of oligosaccharides, the alkali-stable polysaccharide was submitted to partial hydrolysis. The polysaccharide (100 g.) was dissolved in 0·01N-sulphuric acid (10 l.), then the solution was adjusted to pH 2 with N-sulphuric acid and heated in a stoppered vessel at 80° for 22 hr.; during this time, further additions of acid were necessary to maintain pH 2. After cooling, the solution was neutralised with barium carbonate, filtered, and concentrated to *ca.* 0·5 l. Material of high molecular weight was precipitated by the addition of methanol (2 l.), then the supernatant liquid was evaporated, yielding a yellow solid (49 g.). This was dissolved in the minimum volume of water, and the solution percolated through a squat column (18 × 12 cm.) of B.D.H. acid-washed charcoal, which had previously been washed with water (5 l.). Fractions containing monosaccharides were eluted from the column with water and water–ethanol (5 l. each time) (see Table 2); elution with concentrations of ethanol greater than 5% afforded mixtures of oligosaccharides, which were retained for further investigation.

Attempts to isolate the compounds with R_{Rh} 0·39 and 0·71 by chromatography of the whole fraction on large paper sheets were unsuccessful; neither compound was obtained in quantity sufficient for further examination. The compound with R_{Rh} 0·71 was indistinguishable from fucose on paper chromatograms.

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The compounds with R_{Rh} 1·2 and 1·3 resembled 2-*O*-methylxylose and 2-*O*-methylfucose respectively in their chromatographic behaviour. These identifications were confirmed on the materials obtained when the appropriate fractions were submitted to chromatography on large

TABLE 2. *Fractionation of mono- and oligo-saccharides of the sugar-beet polysaccharide.*

Eluent	Weight of fraction (g.)	Components *
Water	39·0	Arabinose (mainly), galactose
Water + 1% v/v EtOH	0·6	Rhamnose
„ 2% „	0·5	Rhamnose + traces of compounds with R_{Rh} 0·39 (pink) and 0·71 (brown)
„ 3% „	0·23	Oligosaccharides + compounds with R_{Rh} 1·2 (pink) and 1·3 (yellow-brown)
„ 4% „	0·37	Oligosaccharides + compounds with R_{Rh} 1·2 (pink) and 1·3 (yellow-brown)
„ 5% „	0·28	Oligosaccharides + compounds with R_{Rh} 1·2 (pink) and 1·3 (yellow-brown)

* R_{Rh} = rate of movement relative to rhamnose in solvent (*b*); colours are those produced on chromatograms sprayed with *p*-anisidine hydrochloride and heated.

paper sheets with solvent (*c*). The monosaccharides were eluted from the requisite areas of the chromatograms with water, then the aqueous solutions were passed through columns of IR-120(H) and IR-400(CO_3) resins, and evaporated to dryness.

2-*O*-Methyl-D-xylose (33 mg.) had $[\alpha]_D$ +24° ± 5° (*c* 1·7) and R_{Rh} 1·22 in solvent (*b*). After recrystallisation from acetone it had m. p. and mixed m. p. 133—134°, and the *X*-ray powder photograph of the compound was identical with that of an authentic specimen.

2-*O*-Methyl-L-fucose (15 mg.) crystallised from acetone, and then had m. p. and mixed m. p. 148—150°, $[\alpha]_D$ −77° ± 3° (*c* 0·7; equil.), and R_{Rh} 1·29 in solvent (*b*). *X*-Ray powder photography confirmed the identification.

Elution with water of further areas of the chromatograms from which the *O*-methyl sugars were obtained gave a compound (24 mg.) which behaved as a uronic acid on the chromatogram; it gave a pink spot with *p*-anisidine hydrochloride, and had R_{Rh} *ca.* 0·2 in solvent (*c*), but apparently was contaminated with inorganic material. After treatment with methanolic hydrogen chloride (2% w/w; 10 c.c.) for 8 hr. under reflux, borohydride reduction, and hydrolysis with 2N-sulphuric acid for 8 hr. at 100°, paper chromatography of the products revealed the presence of galactose and 2-*O*-methylxylose.

Quantitative Analysis of the Alkali-stable Polysaccharide.—The purified polysaccharide (36·8 mg.) was hydrolysed in N-sulphuric acid (2 c.c.) at 100° for 16 hr. D-Ribose (16·5 mg.) was added to the cooled hydrolysate, which was then neutralised with barium carbonate and concentrated. After separation on paper chromatograms [solvent (*a*)], the components of the monosaccharide mixture were estimated colorimetrically and in duplicate by the benzidine method.[13] The results are shown in Table 3, where recoveries are calculated on the basis of the respective ribose estimates.

TABLE 3. *Composition of the alkali-stable polysaccharide.*

Aldose	Found (mg.)	Recovery from polysaccharide, calc. as anhydroaldose (mg.)	(%)	Molar ratios (mean)
Arabinose	4·40, 4·54	27·20, 26·90	74·0, 73·0	21·0
Galactose	0·61, 0·63	3·85, 3·82	10·5, 10·4	3·0
Rhamnose	0·21, 0·21	1·31, 1·26	3·6, 3·4	1·0
Ribose	2·35, 2·45			

The uronic anhydride content of the polysaccharide was estimated by Johansson, Lindberg, and Theander's method [14] (Found: 5·5, 4·8% in duplicate experiments) and by titration of an aqueous solution of the polysaccharide (sulphated ash, 0·8%) with 0·01N-sodium hydroxide, with phenolphthalein as indicator (Found: 5·1%, corresponding to an equivalent weight of 3470 for the polysaccharide).

[13] Jones and Pridham, *Biochem. J.*, 1954, **58**, 288.
[14] Johansson, Lindberg, and Theander, *Svensk Papperstidn.*, 1954, **57**, 41.

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The nitrogen content of the purified polysaccharide (0·8%) indicated a protein content of *ca.* 5% (based on an average N content of 16% for the protein), and this was verified by Goodwin and Morton's spectrophotometric method [15] (Found for the polysaccharide: tyrosine, 0·31; tryptophan, 0·026%). If it is assumed that the protein contains 6% of tyrosine and 0·5% of tryptophan (*e.g.*, albumin of peas), this corresponds to a protein content of 5·2% in the polysaccharide.

Further Experiments with the Alkali-stable Polysaccharide.—The polysaccharide was heated in saturated lime-water at 80° for 24 hr., then isolated, after neutralisation of the solution with acetic acid, by precipitation with ethanol. The optical rotation and composition (determined by paper chromatography of a hydrolysate) of this product were similar to those of the starting material.

An aqueous solution of Cetavlon (20% w/v) was slowly added to a stirred solution (1% w/v) of the polysaccharide (sulphated ash, 0·8%).[16] The small amount of precipitate formed was collected after 24 hr., and the polysaccharide remaining in solution was precipitated with ethanol. Paper-chromatography of hydrolysates of the two fractions indicated that they were similar in composition.

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THE UNIVERSITY, BRISTOL. [*Received, October 30th*, 1958.]

[15] Goodwin and Morton, *Biochem. J.*, 1946, **40**, 628.
[16] Bera, Foster, and Stacey, *J.*, 1955, 3788.

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156. X-*Irradiation of Aqueous Benzene Solutions.*

By J. H. BAXENDALE and D. SMITHIES.

The yields (*G* molecules/100 ev) of phenol, diphenyl, hydrogen peroxide, and hydrogen from *X*-irradiated aqueous benzene solutions have been measured in various conditions. In de-aerated solutions $G(\text{Ph·OH}) = 0·34$, $G(\text{Ph}_2) = 0·55$, and $G(\text{H}_2) = 0·60$, independently of dose and the same in neutral and in 0·1N-sulphuric acid solutions. $G(\text{H}_2\text{O}_2)$ varies with dose, benzene concentration, and acidity owing to the fact that hydrogen peroxide takes part in secondary reactions. In the presence of oxygen $G(\text{Ph·OH})$ and $G(\text{H}_2\text{O}_2)$ increase substantially and $G(\text{Ph}_2)$ falls to zero. Addition of Cu^{2+} and/or Fe^{3+} to de-aerated solutions also increases $G(\text{Ph·OH})$ and decreases $G(\text{Ph}_2)$. There is evidence for unidentified reduction products in the de-aerated solutions, and for other oxidation products in aerated solutions and in solutions containing Cu^{2+} and Fe^{3+}.

THE absorption of ionising radiation by aqueous benzene solution gives mainly phenol and diphenyl in the absence of oxygen, but in air the chief products are phenol and hydrogen peroxide. It has been concluded from previous work [1] that these are formed by the action of H and HO produced from water by the radiation, and investigations using other sources of HO, such as Fenton's reagent [2,3] and ultraviolet-irradiated ferric ion solutions, support this.[4] In the latter study, the reaction of ferric ion with the radicals formed from benzene proved helpful in the elucidation of the reactions involved and it has been used in the work now reported.

EXPERIMENTAL

Materials.—Benzene of A.R. grade was purified by recrystallisation. Solutions of Cu^{2+} and Fe^{3+} were made up from A.R. copper sulphate and ferric ammonium sulphate. Reaction

[1] Stein and Weiss, *J.*, 1949, 3245.
[2] Merz and Waters, *ibid.*, p. 2427.
[3] Baxendale and Magee, *Discuss. Faraday Soc.*, 1953, **14**, 160.
[4] *Idem, Trans. Faraday Soc.*, 1955, **51**, 205.

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mixtures were made up in water distilled once from a glass still. Further purification using alkaline permanganate or by photolysing hydrogen peroxide in the water had no effect. This is not surprising since with the relatively large concentrations of benzene used in the reactions, any effect due to traces of impurities will be negligible.

Irradiation Apparatus.—Solutions, usually 250 c.c. in 750 c.c. flasks, were exposed to the unfiltered radiation from a Siemens constant-potential *X*-ray tube run at 190 kv and 12 ma. In order to calculate the energy absorbed by the solution in the flask, three tubes containing 10^{-3}M-ferrous sulphate in 0·8N-sulphuric acid were exposed at the same time as the flask. The relative doses given to the flask and tubes were obtained by previous calibration experiments in which the flask contained a ferrous sulphate solution containing the same concentration of sulphuric acid as that used in the reaction mixtures. Yields reported previously [5,6] on this system are in error because the absorption by sulphuric acid was not taken into account. For reactions in the absence of acid, the energy absorbed was calculated from a calibration with ferrous sulphate in 0·1N-sulphuric acid. This was corrected (by about 2%) for the extra absorption of sulphuric acid, the results of observations at different acid concentrations being used. All doses were calculated on the basis of 15·6 molecules of Fe^{3+} formed per 100 ev absorbed by ferrous sulphate solution.

Analyses.—The methods used to estimate hydrogen, Fe^{3+}, and hydrogen peroxide have been given elsewhere.[6] Diphenyl was extracted from the reaction mixture by hexane, and phenol by ether, and the amounts of each were obtained by ultraviolet absorption, the methods described previously [4] being used.

Results.—De-aerated solutions. In the absence of oxygen no products other than phenol, diphenyl, hydrogen peroxide, and hydrogen could be detected by the analytical methods used. The 100 ev yields of these at different acidities, doses, and benzene concentrations are given in Tables 1 and 2. Phenol and hydrogen are almost constant throughout, but the diphenyl and

TABLE 1. *Yields in de-aerated aqueous solutions saturated with benzene.* Dose rate *ca.* 5×10^{19} ev $l.^{-1}$ $min.^{-1}$.

Conditions	Dose (10^{21} ev/l.)	$G(Ph_2)$	$G(Ph{\cdot}OH)$	$G(H_2O_2)$	$G(H_2)$
Neutral	0·39	—	—	0·34	—
	0·74	0·59	0·33	0·29	0·60
	1·41			0·20	0·60
	1·50	0·57	0·30	0·19	
	2·16		0·16		
	2·83		0·13		
0·01N-H_2SO_4	0·71	0·59	0·35	0·60	—
	1·56	0·56	0·33	0·59	
	2·82	0·53	0·36		0·60
0·1N-H_2SO_4	0·78	0·52	0·32	0·58	0·58
	1·53	0·55	0·35	0·61	
	1·70	0·55	0·32	0·59	
0·8N-H_2SO_4	1·66	0·44	0·30	0·51	0·52
0·1N-NaOH	1·46	0·45	0·35	0·40	0·63

TABLE 2. *Effect of benzene concentration on the yields in de-aerated neutral solution.* Dose rate *ca.* 5×10^{19} ev $l.^{-1}$ $min.^{-1}$. Total dose *ca.* 7×10^{20} ev $l.^{-1}$.

10^3[Benzene]	22 *	4·6	4·5	4·0	3·8
$G(Ph_2)$	0·59	0·55	0·53	0·57	0·56
$G(Ph{\cdot}OH)$	0·33	0·30	0·31	0·32	0·34
$G(H_2O_2)$	0·29	0·19	0·19	0·21	0·20

* Means of seven determinations having maximum deviations of $\gtrless 5\%$.

hydrogen peroxide yields show some variations. In particular $G(H_2O_2)$ decreases with dose. This suggests that, in neutral (and possibly also in alkaline) solution, reactions occur to remove hydrogen peroxide, and this is confirmed by the effect produced by having hydrogen peroxide present initially. Thus with $1{\cdot}6 \times 10^{-3}$M-hydrogen peroxide in neutral solution, $G(H_2O_2) = -0{\cdot}27$ for a total dose of $1{\cdot}8 \times 10^{21}$ ev/l., *i.e.*, more is removed than formed, while $G(Ph_2)$ and

[5] Baxendale and Smithies, *J. Chem. Phys.*, 1955, **23**, 604.
[6] *Idem, Z. phys. Chem.* (*Frankfurt*), 1956, **7**, 241.

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G(Ph·OH) are increased to 0·64 and 0·31 respectively. In contrast, hydrogen peroxide has no effect on the yields in 0·01N-sulphuric acid.

The values of $G(H_2)$ and G(Ph·OH) agree fairly well with previous work.[1,7,8] Stein and Weiss [1] found about the same value for $G(Ph_2)$ but Phung and Burton [8] report higher values. In acid, $G(H_2O_2)$ agrees with other determinations,[7,8] but in neutral solution $G(H_2O_2) = 0$ has been reported,[7,8] compared with 0·4 obtained by extrapolation of our results to zero dose. There seems little doubt that the earlier value is in error because of the much larger doses used.

Aerated solutions. Previous work showed that G(Ph·OH) increases appreciably in the presence of air. This is evident from Table 3, which also shows a considerable increase in

TABLE 3. *Yields in neutral saturated aqueous benzene solutions with oxygen present.* Total dose *ca.* 10^{21} ev/l.

Gas phase	G(Ph·OH)	$G(Ph_2)$	$G(H_2O_2)$
1 atm. O_2	1·56	0·03	2·62
1 atm. air	1·57	0·03	2·50
20 cm. air	1·50	0·07	2·44

$G(H_2O_2)$ and decrease in $G(Ph_2)$. There is also evidence for other products, since the ether extract of the irradiated solutions absorbs much more at 290 mμ than would be expected if it contained only phenol. The additional absorption is removed by aqueous sodium hydrogen carbonate, and the bicarbonate solution then has a broad absorption band with a peak at *ca.* 265 mμ which increases slightly when the solution is made alkaline and disappears when it is made acid. This behaviour is reversible and indicates the presence of an acidic material which is stable to alkali and oxygen. The contribution of this material to the absorption maximum of phenol at 274 mμ was usually about 15%, so that before measurement at 274 mμ the ether extract was washed with ether-saturated aqueous sodium hydrogen carbonate.

In similar conditions, using higher doses, Daniels *et al.*[9] reported the presence of a substance with properties resembling mucondialdehyde and discussed the mechanism of its formation. We found none of these further oxidation products in deærated solutions.

Typical yields in air and oxygen are given in Table 3. Table 4 shows that in acid the hydrogen peroxide yield is higher than in alkali but that both decrease with dose. In all the

TABLE 4. *Hydrogen peroxide yields in aerated solutions saturated with benzene.*

Dose (10^{20} ev/l.)	6	18	24
$G(H_2O_2)$ in 0·1N-H_2SO_4	3·30	3·14	3·02
$G(H_2O_2)$ in neutral solution	2·50	2·28	2·20

experiments the doses given are insufficient to exhaust the oxygen in solution. Analysis of the solutions at intervals up to 24 hr. after irradiation did not reveal any post-irradiation changes in phenol and hydrogen peroxide concentrations which have been reported.[10] In comparison with other work [7,8,9,11] our G(Ph·OH) values are much lower, and we suggest that the product mentioned above interferes with the analytical methods used previously—particularly those depending on the absorption of the phenol in the irradiated solution.[7,8] Our $G(H_2O_2)$ values are higher in acid and lower in neutral solution than those of Phung and Burton.[8]

Yields in the presence of metal ions. The effect of metal ions on *X*-irradiated aqueous benzene is shown in Table 5. Although the phenol increases as Fe^{3+} is added as in the photochemical system, unlike in the latter the diphenyl yield increases at first and then decreases at higher concentration of Fe^{3+}. The yields of phenol, Fe^{2+}, and benzene oxidised, G(PhH), all increase and appear to approach limiting values at high metal-ion concentrations. $G(H_2)$ is almost constant throughout and is of the order usually obtained for the so-called molecular yield.

[7] Sworski, *J. Chem. Phys.*, 1952, **20**, 1817; *Radiation Res.*, 1954, **1**, 231.
[8] Phung and Burton, *Radiation Res.*, 1957, **7**, 199.
[9] Daniels, Scholes, and Weiss, *J.*, 1956, 832.
[10] Wright, *Discuss. Faraday Soc.*, 1952, **12**, 114.
[11] Freeman, Van Cleave, and Spinks, *Canad. J. Chem.*, 1953, **31**, 448.

If diphenyl, phenol, hydrogen, and Fe^{2+} are the only products in these conditions then we should have

$$2G(Ph_2) + 2G(Ph{\cdot}OH) = 2G(H_2) + G(Fe^{3+})$$

The observations in de-aerated solutions without metal ions (Table 1) show a deficiency of reduction products. The results in Table 5 show that this deficiency decreases when metal

TABLE 5. *Irradiations in the presence of* Cu^{2+} *and/or* Fe^{3+}. Dose rate *ca.* 5×10^{19} ev $l.^{-1}$ $min.^{-1}$. Total dose *ca.* $1{\cdot}5 \times 10^{21}$ ev/l. Solutions saturated with benzene and 0·1N in H_2SO_4.

Initial $[Fe^{3+}]$ $(10^{-4}M)$	$[Cu^{2+}]$ $(10^{-4}M)$	$G(Fe^{3+})$	$G(Ph_2)$	$G(Ph{\cdot}OH)$	$G(PhH)$	$G(H_2)$
—	—	—	0·55	0·33	1·43	0·58
0·2	—	0·63	1·00	0·36	2·36	—
0·56	—	2·15	1·12	0·43	2·67	—
1·0	—	2·51	1·18	0·52	2·88	0·53
5·0	—	3·20	0·91	0·92	2·74	—
5·0	1·0	4·70	0·41	2·16	2·98	—
5·0	5·0	6·07	0·16	2·98	3·30	—
5·0	10	6·32	0·12	3·10	3·34	—
5·0	20	6·07	0·10	3·20	3·40	0·57

ions are added and becomes a deficiency in oxidation products amounting to about 10%. This persists even at the highest metal-ion concentration, where it seems likely that all the radicals produced will be caught by either metal ion or benzene. A similar deficiency was observed in the photochemical oxidation, although in the oxidation by Fe^{2+} and hydrogen peroxide good balances were obtained by the same analytical method.[3] It appears that undetected oxidation products are present in the photochemical and *X*-irradiation systems.

DISCUSSION

The following reactions are generally agreed to occur on the irradiation of de-aerated aqueous benzene:

$$H_2O \longrightarrow H,\ HO,\ H_2,\ H_2O_2$$
$$HO + PhH \longrightarrow Ph{\cdot} + H_2O \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$2Ph{\cdot} \longrightarrow Ph_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$
$$Ph{\cdot} + OH \longrightarrow Ph{\cdot}OH$$
$$PhH + H \longrightarrow C_6H_7$$

The yields of phenol, diphenyl, and hydrogen peroxide are together much bigger than that of hydrogen, which is the only reduction product measured so far. This deficiency is no doubt due to the presence of undetected partially hydrogenated benzenes and possibly diphenyls which, as previously suggested,[1] originate from C_6H_7 by the further addition of hydrogen atoms or by dimerisation. However, even the yields of benzene oxidation products (~0·9 molecule/100 ev) are less than would be expected if all the HO produced (~3 radicals/100 ev) is used in oxidation, and this may be accounted for by the back reaction:

$$Ph{\cdot} + H \longrightarrow PhH \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Both these suggestions are supported by the present observations on the effect of Fe^{3+} and Cu^{2+} on the products. By analogy with the photochemical oxidation by $Fe^{3+}OH$, the reactions

$$H_2O + Ph + Fe^{3+} \longrightarrow Ph{\cdot}OH + Fe^{2+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$
$$H_2O_2 + Fe^{2+} \longrightarrow Fe^{3+} + OH^- + HO$$

are to be expected, as well as

$$Fe^{2+} + H \longrightarrow Fe^{3+} + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

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which has been shown to occur in the *X*-irradiation of other aqueous systems.[6] Reactions (4) and (5) will reduce both the formation of partially hydrogenated compounds and the extent of the back reaction (3), so that G(Ph·OH) and the amount of benzene reacting, G(PhH), are increased as shown in Table 5. The increase in $G(Ph_2)$ at low Fe^{3+} concentrations probably results from the increase in phenyl-radical concentration brought about by the suppression of reaction (3), while the decrease in $G(Ph_2)$ at higher metal-ion concentrations can be attributed to prevention of reaction (2) by reaction (4).

The occurrence of reactions (1)—(5) means that at high Fe^{3+} or Cu^{2+} concentrations the only reactions of H and Ph· will be with the metal ion, so that $G(Ph_2)$ should approach zero, and G(Ph·OH) and $G(Fe^{2+})$ should approach limiting values. In these conditions, phenol and diphenyl being assumed to be the only oxidation products, we should have $G(\text{Ph·OH}) = G_w(\text{HO}) + G_w(H_2O_2)$; $G(Fe^{2+}) = G_w(\text{H}) + G_w(\text{HO})$, where G_w denotes a primary yield.

Table 5 shows that even at the highest metal-ion concentrations a little diphenyl is still formed and G(Ph·OH) is increasing slightly so that the above conditions have not quite been attained. However, as pointed out above, even at low Fe^{3+} concentrations reduction of Fe^{3+} by hydrogen atoms occurs, so that it seems likely that all the latter will be removed by this reaction at the higher concentrations. Assuming this, we have

$$G(\text{Ph·OH}) + 2G(Ph_2) + G_w(\text{HO}) + G_w(H_2O_2) \quad \text{(i)}$$

and

$$G(Fe_2^{+}) + 2G(Ph_2) = G_w(\text{H}) + G_w(\text{HO}) \quad \text{(ii)}$$

These equations ignore the undetected oxidation products. If these are formed *via* radicals which are oxidised by the metal ion, then equation (ii) will be unchanged but the yield of the product should be included in (i) with those of phenol and diphenyl. This yield will be given by the deficiency of oxidation products in the balance. The yields being taken at the highest metal-ion concentration, the deficiency amounts to 0·35, $G(H_2) = 0{\cdot}6$, $G(Fe^{2+}) = 6{\cdot}1$, G(Ph·OH) = 3·2, and $G(Ph_2) = 0{\cdot}1$. Hence

$$G_w(\text{HO}) + G_w(H_2O_2) = 3{\cdot}75$$
$$G_w(\text{H}) + G_w(\text{HO}) = 6{\cdot}3$$

Assuming $G_w(H_2O_2) = 0{\cdot}6$, which is found in acid solution without metal ions, we have

$$G_w(\text{HO}) = G_w(\text{H}) = 3{\cdot}15; \quad G_w(H_2) = G_w(H_2O_2) = 0{\cdot}6$$

which are similar to primary yields previously reported.[12]

THE UNIVERSITY, MANCHESTER. [*Received, November 18th,* 1958.]

[12] Hochanadel and Lind, *Ann. Rev. Phys. Chem.*, 1956, **7**, 83.

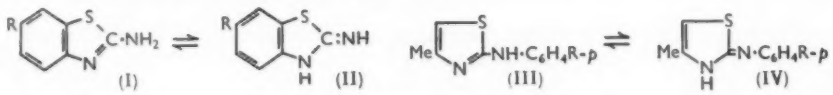
157. *The Unsaturation and Tautomeric Mobility of Heterocyclic Compounds. Part XIII.* The Methylation of Some Amino-thiazole Derivatives.*

By R. F. Hunter, E. R. Parken, and Eileen M. Short.

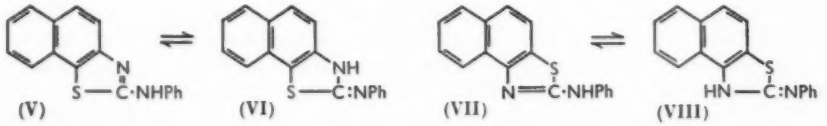
6-Substituted 2-aminobenzothiazoles [1] and 2-(*p*-substituted anilino)-4-methylthiazoles [2] which apparently react wholly in the amino-aromatic form with dimethyl sulphate and methyl iodide alone, to give iminomethylthiazoline derivatives, yield mixtures of methyl isomers corresponding to both tautomeric forms in the presence of ethanolic sodium ethoxide. 2-Anilinonaphtho-[2,1]- and -[1,2]-thiazole similarly give greatly enhanced proportions of the methylaminothiazole derivatives formed in small amount with methyl iodide alone.

The methylation of representative 6-substituted 2-aminobenzothiazoles [1] (I ⇌ II) and 2-(*p*-substituted anilino)-4-methylthiazoles [2] (III ⇌ IV), which apparently react exclusively in the amino-aromatic form to give 2-imino-3-methyl- and 2-arylimino-3 : 4-dimethyl-thiazolidine derivatives, have been re-examined in respect of the influence of ethoxide ions. As might be expected from the results obtained with 6-substituted, 6 : 4′-disubstituted, and 4′-substituted 2-anilinobenzothiazoles,[3] ethoxide ions cause substantial methylation on the non-nuclear nitrogen atom of the semicyclic amidine system, leading to pairs of isomeric methyl derivatives in accordance with " classical tautomerism."

Methylation of 2-amino-6-methylbenzothiazole (I ⇌ II; R = Me) in ethanolic sodium ethoxide in the presence of a large excess of dimethyl sulphate gave a 2 : 3 mixture of 2-methylamino-6-methylbenzothiazole and 2-imino-3 : 6-dimethylbenzothiazoline. The 6-chloro- and the 6-bromo-derivative (I ⇌ II; R = Cl or Br) gave respectively 1 : 2 and 1 : 4 mixtures of the corresponding isomers.



4-Methyl-2-*p*-toluidinothiazole (III ⇌ IV; R = Me) with methyl iodide and an excess of ethanolic sodium ethoxide gave a mixture of 2-*p*-tolylimino-3 : 4-dimethyl- and 2-*p*-tolylmethylamino-4-methyl-thiazole (the ratio could not be estimated on account of gum-formation). 2-*p*-Chloro- and 2-*p*-bromo-anilino-4-methylthiazole (III ⇌ IV; R = Cl and Br) gave respectively 4 : 1 and 5 : 2 mixtures in which the 3 : 4-dimethylthiazolines predominated.



2-Anilinonaphtho[2,1]thiazole (V ⇌ VI) with methyl iodide alone, which was previously reported [4] to yield solely the 3-methyl-2-phenyliminonaphthothiazoline, gives actually ~12% of 2-*N*-methylanilino-isomer, but in the presence of ethanolic sodium ethoxide this slightly predominated.

* Part XII, *J.*, 1958, 1561.

[1] Hunter and Jones, *J.*, 1930, 2190; Dyson, Hunter, Jones, and Styles, *J. Indian Chem. Soc.*, 1931, **8**, 147.

[2] Hunter and Parken, *J.*, 1934, 1175.

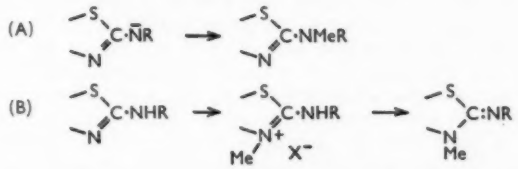
[3] Hunter, Parken, and Short, *J.*, 1958, 1561.

[4] Chowdhury, Desai, and Hunter, *J. Indian Chem. Soc.*, 1933, **10**, 637.

XUM

2-Anilinonaphtho[1,2]thiazole (VII ⇌ VIII) with methyl iodide alone was also found to give more (*ca.* 10%) 2-methylanilino-isomer than was originally reported.[5] In the presence of ethanolic sodium ethoxide, the ratio of isomers was reversed in favour of the 2-methylanilino-derivative.

The effect of ethoxide ions in causing the appearance of methylamino-isomers, or in greatly enhancing their proportion, is interpreted as resulting mainly from superposition of an " amide " mechanism (A) of methylation of the ion derived from the amino-aromatic



form by deprotonation on the " ammonium " mechanism (B) pictured for methylation of the base itself in the presence of methyl iodide or dimethyl sulphate alone. It appears feasible, however, that the formation of pairs of isomeric methyl derivatives in methylation by methyl iodide alone may arise from methylation by the " ammonium " mechanism of actual tautomerides as pictured by Hunter and Styles in 1928 [6] on the basis of Pyman's experiments on the addition of methyl iodide to " mobile " and " static " amidines.[7] The iminothiazoline tautomer which gives rise to the methylamino-isomer is derived from the original single individual which has the amino-aromatic structure (ultraviolet spectroscopical evidence) by a mechanism involving prototropy under the influence of solvating methyl iodide molecules which are present in substantial excess.

[*Added, November 30th,* 1958.—Distribution of charge will of course cause production to some extent of the isomeric ion having an exocyclic imino-group and a negative charge on the ring nitrogen atom. This should, however, be small since the stability will be lower on account of the use of an electron of the aromatic sextet for the αβ double bond, which therefore breaks the aromatic resonance. It is not suggested that the ions of the tautomers necessarily exist as actual entities; the deprotonated system is probably best symbolised by a sharing of the negative charge between the two nitrogen atoms.]

Experimental

2-Amino-6-methylbenzothiazole.—The base, m. p. 142°, prepared from *N-p*-tolylthiourea and bromine,[8] gave a pale yellow *picrate* in acetone which, crystallised from ethyl acetate, had m. p. 280—281° (Found: S, 7·9. $C_8H_8N_2S,C_6H_3O_7N_3$ requires S, 8·1%).

Methylation by dimethyl sulphate in ethanolic sodium ethoxide. The base (2 g.) in ethanolic sodium ethoxide (prepared from 2·3 g. of sodium in 50 ml. of ethanol) was heated with dimethyl sulphate (10 ml.) under reflux for 4 hr., treated with excess of ammonia (*d* 0·880) after removal of the bulk of the alcohol, and extracted with chloroform. The gum recovered from an ethanolic solution of the product by concentration under reduced pressure at room temperature was stirred with cold acetone. The residue (0·5 g.), when washed with ether and recrystallised from boiling water, gave 2-amino-6-methylbenzothiazole (0·2 g.), m. p. and mixed m. p. 141—142°. The gum (1·1 g.) recovered from the acetone extraction was converted into a mixture of picrates which on fractional crystallisation furnished 6-methyl-2-methylaminobenzothiazole picrate (0·7 g.) which after recrystallisation from ethyl acetate (charcoal) had m. p. 255° and 255—256° on admixture with a specimen prepared from the synthetic base, and *2-imino-3 : 6-dimethylbenzothiazoline picrate* (1·1 g.), m. p. 221° (from ethyl acetate; charcoal) and 219—220° when mixed with a specimen prepared from the synthetic base (Found: S, 7·65. $C_9H_{10}N_2S,C_6H_3O_7N_3$ requires S, 7·9%). 2-Imino-3 : 6-dimethylbenzothiazoline, prepared from

[5] Desai, Hunter, and Kureishy, *J.*, 1936, 1668.
[6] Hunter and Styles, *J.*, 1928, 3019.
[7] Burtles and Pyman, *J.*, 1923, **123**, 362; Pyman, *ibid.*, pp. 367, 3359.
[8] Hunter, *J.*, 1926, 1385.

N-methyl-*N*-*p*-tolylthiourea and bromine, gave a *picrate*, yellow needles, m. p. 220—221° (from ethyl acetate) (Found: S, 7·7%). 2-Methylamino-6-methylbenzothiazole, m. p. 152°,[1] prepared from *N*-methyl-*N'*-*p*-tolylthiourea and bromine, gave a *picrate*, yellow needles, m. p. 256—257° (from ethyl acetate) (Found: S, 7·7%).

2-*Amino*-6-*chlorobenzothiazole*.—The *picrate* of this base crystallised from ethyl acetate in pale yellow needles, m. p. 271° (Found: S, 7·65. $C_7H_5N_2ClS,C_6H_3O_7N_3$ requires S, 7·7%). The base (2 g.) was methylated in ethanolic sodium ethoxide (50 ml.) with dimethyl sulphate (10 ml.). A residue (0·2 g.) remaining after extraction with chloroform was unchanged base (m. p. and mixed m. p. 196°). The gum was converted into mixed picrates which on crystallisation from ethyl acetate gave the picrate of unchanged base (1 g.; m. p. and mixed m. p. 271°), 6-chloro-2-imino-3-methylbenzothiazoline picrate (1·55 g.) (which on recrystallisation had m. p. 239—240° and 239° when mixed with a specimen prepared from the synthetic base), and 6-chloro-2-methylaminobenzothiazole picrate (0·8 g.) (which on recrystallisation had m. p. 230° and 229—230° when mixed with a specimen prepared from the synthetic base).

N-p-*Chlorophenyl*-N-*methylthiourea*, prepared from *p*-chloro-*N*-methylaniline (3·5 g.), potassium thiocyanate (2·5 g.), and hydrochloric acid (3 ml.) in aqueous ethanol, crystallised from ethanol in prisms, m. p. 125° (1·7 g.) (Found: S, 16·1. $C_8H_9N_2ClS$ requires S, 16·0%). 6-Chloro-2-imino-3-methylbenzothiazoline obtained by heating the thiourea (1 g.) with bromine (1 ml.) in chloroform (12 ml.) under reflux for 10 min., crystallised from methanol in plates, m. p. 79°. The yellow *picrate*, prepared in acetone and crystallised from ethyl acetate, had m. p. 239° (Found: Cl, 8·4; S, 7·3. $C_8H_7N_2ClS,C_6H_3O_7N_3$ requires Cl, 8·3; S, 7·4%).

6-*Chloro*-2-*methylaminobenzothiazole*, m. p. 214°, prepared from *N*-*p*-chlorophenyl-*N'*-methylthiourea and bromine,[1] gave a *picrate*, needles (from ethyl acetate), m. p. 230—231° (Found: S, 7·3. $C_8H_7N_2ClS,C_6H_3O_7N_3$ requires S, 7·4%).

2-Amino-6-bromobenzothiazole, prepared by bromination of 2-aminobenzothiazole in chloroform,[9] gave a *picrate*, m. p. 273° (from ethyl acetate) (Found: S, 6·9. $C_7H_5N_2BrS,C_6H_3O_7N_3$ requires S, 7·0%). The base (2 g.) was treated in ethanolic sodium ethoxide (40 ml.) with dimethyl sulphate (10 ml.), and the gum was converted into a mixture of picrates. Fractionation from acetone and then from ethyl acetate yielded picrate of unchanged base (0·6 g.; m. p. 272°; mixed m. p. 272—273°), 6-bromo-2-imino-3-methylbenzothiazoline picrate (3 g.) (on recrystallisation from ethyl acetate, m. p. 240° and 239—240° when mixed with a specimen obtained from the synthetic base), and 6-bromo-2-methylaminobenzothiazole picrate (0·6 g.) (after recrystallisation, m. p. and mixed m. p. 236°).

6-Bromo-2-imino-3-methylbenzothiazoline, m. p. 110°, prepared by bromination of the 2-imino-3-methyl base, gave a *picrate*, yellow needles, m. p. 240° (from ethyl acetate) (Found: S, 6·9. $C_8H_7N_2BrS,C_6H_3O_7N_3$ requires S, 6·8%).

6-Bromo-2-methylaminobenzothiazole, prepared from *N*-*p*-bromophenyl-*N'*-methylthiourea and bromine, crystallised from ethanol in needles, m. p. 224°. The *picrate*, prepared in acetone, crystallised from ethyl acetate in pale yellow needles, m. p. 231° (Found: S, 6·7%).

2-Anilinonaphtho[2,1]thiazole, prepared from *N*-β-naphthyl-*N'*-phenylthiourea and bromine,[10] had m. p. 211—212°. The *picrate*, prepared in benzene, crystallised from alcohol in pale yellow needles, m. p. 253° (Found: S, 6·5. $C_{17}H_{12}N_2S,C_6H_3O_7N_3$ requires S, 6·3%). (i) The base (5 g.) was heated with methyl iodide (7·5 ml.) at 100° for 12 hr., the product digested with hot 33% aqueous potassium hydroxide and extracted with chloroform, and the gummy base was stirred with cold absolute ethanol. The residue of 3-methyl-2-phenyliminonaphtho[2,1]-thiazoline (4 g.) had m. p. 183° (185—186° on recrystallisation from ethanol) and at 186° when mixed with a specimen synthesised from *N*-methyl-*N*-β-naphthyl-*N'*-phenylthiourea. A solution of the gum (0·9 g.) recovered from the alcoholic extract in benzene gave 1·1 g. of 1-*N*-methylanilinonaphtho[2,1]thiazole picrate in four fractions which after recrystallisation had m. p. 184° alone and when mixed with a specimen prepared from the synthetic base. (ii) The gum obtained by heating the base (4 g.), methyl iodide (6 ml.), and ethanolic sodium ethoxide (6 ml.) under the same conditions gave on stirring with cold absolute ethanol 3-methyl-2-phenyliminonaphtho[2,1]thiazoline (1·45 g.) which after recrystallisation had m. p. 184—185° and mixed m. p. 185°. The picrate from the recovered gum yielded a total of 3·15 g. of 1-*N*-methylanilinonaphtho[2,1]thiazole picrate which on recrystallisation from ethanol (charcoal) had m. p. and mixed m. p. 186—187°.

[9] Hunter, *J.*, 1930, 125.
[10] Hunter and Jones, *J.*, 1930, 941.

N-Methyl-N-β-naphthyl-N'-phenylthiourea, prepared from phenylthiocarbimide and *N*-methyl-β-naphthylamine, had m. p. 108—109° (from ethanol; charcoal) (Found: S, 11·0. $C_{18}H_{16}N_2S$ requires S, 11·0%).

3-Methyl-2-phenyliminonaphtho[2,1]thiazoline, obtained by cyclisation of the thiourea (2 g.) with bromine (0·8 ml.) and crystallised from ethanol, had m. p. 186—187°. The *picrate*, prepared in benzene, had m. p. 217—218° (Found: S, 6·0. $C_{18}H_{14}N_2S,C_6H_3O_7N_3$ requires S, 6·2%).

2-Anilinonaphtho[1,2]thiazole was conveniently prepared from a solution of *N*-α-naphthyl-*N'*-phenylthiourea (6 g.) and bromine (2·4 ml.) in chloroform (68 ml.) and crystallised from ethanol in needles, m. p. 143° alone and when mixed with a specimen prepared from 2-chloronaphtho[1,2]thiazole and aniline (yield, 5 g.). (i) The base (4 g.) was heated with methyl iodide (6 ml.) at 100° for 12—15 hr. Fractionation of the picrate obtained from the gum gave 4 g. of crude 3-methyl-2-phenyliminonaphtho[1,2]thiazoline, m. p. 184° (3·3 g. of m. p. and mixed m. p. 202—203° after extraction with boiling ethyl acetate), and 0·6 g. of 2-*N*-methylanilinonaphtho[1,2]thiazole picrate (m. p. 152—154° and 155—156°; m. p. and mixed m. p. 156° after recrystallisation), and picrate of unmethylated base. (ii) The gum obtained by heating the base (5 g.), methyl iodide (7·5 ml.), and ethanolic sodium ethoxide (7·5 ml.) at 100° for 12 hr. gave with cold absolute ethanol 2-methylanilinonaphtho[1,2]thiazole (3·2 g.), m. p. 113—114° (114—115° after recrystallisation). The recovered gum (1·2 g.) yielded 1·2 g. of 3-methyl-2-phenyliminonaphtho[1,2]thiazoline picrate (m. p. 190; 203° after recrystallisation) and 0·6 g. of 2*N*-methylanilinonaphtho[1,2]thiazole picrate (m. p. and mixed m. p. 154—155° after recrystallisation).

N-Methyl-N-α-naphthyl-N'-phenylthiourea, prepared from phenylthiocarbimide and *N*-methyl-α-naphthylamine, crystallised from ethanol in prisms, m. p. 158—159° (Found: S, 11·0. $C_{18}H_{16}N_2S$ requires S, 11·0%). *3-Methyl-2-phenyliminonaphtho[1,2]thiazoline* obtained by cyclisation of the thiourea (2 g.) with bromine (0·8 ml.), crystallised from ethanol (charcoal) in needles, m. p. 152° (Found: S, 11·1. $C_{18}H_{14}N_2S$ requires S, 11·0%). The picrate prepared in benzene solution had m. p. 203°.

4-Methyl-2-*p*-toluidinothiazole, m. p. 127—128°, prepared from *p*-tolylthiourea and monochloroacetone, gave a *picrate*, needles, m. p. 193—194° (from ethanol) (Found: S, 7·4. $C_{11}H_{12}N_2S,C_6H_3O_7N_3$ requires S, 7·4%).

The base (5 g.), methyl iodide (7·5 ml.), and ethanolic sodium ethoxide (10 ml.) were heated at 100° for 6 hr., the product was digested with 33% aqueous potassium hydroxide, and the mixture diluted with water and extracted with chloroform. When stirred with cold ethanol, the resulting gum gave 3 : 4-dimethyl-2-*p*-tolyliminothiazoline (0·2 g.), m. p. and mixed m. p. 108° (after recrystallisation). The uncrystallisable gum was converted in acetone into a picrate which with benzene gave 1·9 g. of 3 : 4-dimethyl-2-*p*-tolyliminothiazoline picrate (after recrystallisation, m. p. 138°; 138—139° when mixed with a synthetic specimen) and 1·1 g. of 4-methyl-2-*N*-methyl-*p*-toluidinothiazole picrate (after recrystallisation, m. p. and mixed m. p. 176°). The *picrate* obtained from 3 : 4-dimethyl-2-*p*-tolyliminothiazoline which had been prepared from *N*-methyl-*N'*-*p*-tolylthiourea and monochloroacetone, on crystallisation from benzene and then ethanol, formed pale yellow needles, m. p. 139° (Found: S, 7·2. $C_{12}H_{14}N_2S,C_6H_3O_7N_3$ requires S, 7·2%). The *picrate* obtained from 4-methyl-2-*N*-methyl-*p*-toluidinothiazole which had been prepared from *N*-methyl-*N*-*p*-tolylthiourea, crystallised in yellow prisms, m. p. 176° (Found: S, 7·3%).

2-*p*-Chloroanilino-4-methylthiazole, m. p. 147°, gave a *picrate*, m. p. 218° (Found: S, 7·2. $C_{10}H_9N_2ClS,C_6H_3O_7N_3$ requires S, 7·1%). A mixture of the base (5 g.), ethanolic sodium ethoxide (7·5 ml.) and methyl iodide (7·5 ml.) was heated at 100° for 6 hr., then basified with 33% aqueous potassium hydroxide, and the gum (5·1 g.) extracted with chloroform, which showed no signs of crystallisation after 2 days *in vacuo*, converted into a mixture of gummy picrates which were washed with cold ethanol. The residue (6 g.) on fractional crystallisation from ethanol furnished 2-*p*-chlorophenylimino-3 : 4-dimethylthiazoline picrate (4·2 g.) and 2-*p*-chlorophenylmethylamino-4-methylthiazole picrate (1·4 g.) which had m. p. 159—160° unaltered by recrystallisation from ethanol and admixture with a specimen prepared from the synthetic base. The original ethanolic extract furnished a further 0·4 g. of 2-*p*-chlorophenylimino-3 : 4-dimethylthiazoline picrate (m. p. 138—139° and 132—135° after fractionation from benzene; total, 0·35 g.), and the gum (3·2 g.) obtained by evaporation of the mother-liquors was washed repeatedly with cold ethanol, giving a further 1·5 g. of the picrate, m. p. 134—135°.

XUM

The united fractions of 2-*p*-chlorophenylimino-3 : 4-dimethylthiazoline picrate on recrystallisation from ethanol formed needles, m. p. and mixed m. p. 138—139°. 2-*p*-Chlorophenylmethylamino-4-methylthiazole, prepared by condensation of *N*-*p*-chlorophenyl-*N*-methylthiourea (0·8 g.) and monochloroacetone (0·4 ml.), formed a gum (1 g.) whose *picrate*, prepared in acetone, crystallised from ethanol (charcoal) in orange-brown needles, m. p. 159° (Found: Cl, 7·8; S, 6·7. $C_{11}H_{11}N_2ClS,C_6H_3O_7N_3$ requires Cl, 7·6; S, 6·8%).

2-*p*-Bromoanilino-4-methylthiazole, m. p. 162°, gave a *picrate*, m. p. 219° (Found: S, 6·4. $C_{10}H_9N_2BrS,C_6H_3O_7N_3$ requires S, 6·4%).

The gum obtained from the base (5 g.), methyl iodide (7·5 ml.), and ethanolic sodium ethoxide (7·5 ml.) was converted into a mixture of picrates. The first crop consisted of 2-*p*-bromophenylimino-3 : 4-dimethylthiazoline picrate (5·3 g.) which on recrystallisation from benzene gave fractions, m. p. 154—155° (3·7 g.) and m. p. 150—152° (1·4 g.). The mother-liquors, on concentration, furnished crops which on refractionation from ethanol gave 2-*p*-bromophenylmethylamino-4-methylthiazole picrate (2·1 g.), m. p. 161—162° after recrystallisation (Found: Br, 15·8; S, 6·3. $C_{11}H_{11}N_2BrS,C_6H_3O_7N_3$ requires Br, 15·6; S, 6·3%), and the picrate of unchanged base (0·3 g.), m. p. and mixed m. p. 219°.

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158. *Modified Steroid Hormones. Part X.*[1] *Some New Œstradiol Derivatives.*

By D. N. KIRK and V. PETROW.

Application is described of the "dienone–phenol" and the "heterophenol" rearrangement to some steroids having a chlorine atom or a methyl group in ring A.

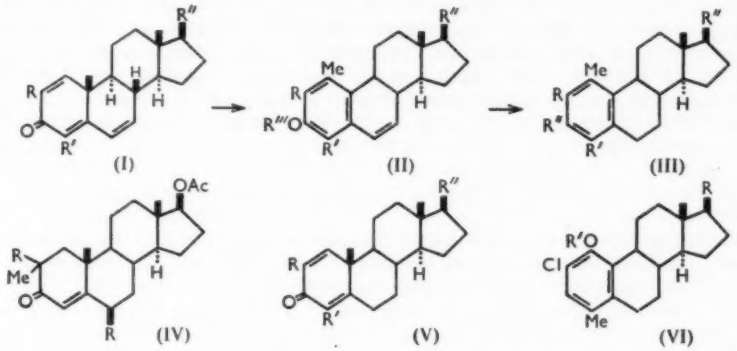
PART IX [1] described the preparation of some chloro-1 : 4-dien-3-ones and -1 : 4 : 6-trien-3-ones of the androstane and the cholestane series. Their conversion into aromatic structures is now reported.

2- (I; R = Cl, R′ = H, R″ = C_8H_{17}) and 4-Chlorocholesta-1 : 4 : 6-trien-3-one (I; R = H; R′ = Cl, R″ = C_8H_{17}) passed smoothly, albeit sluggishly, into 3-acetoxy-2-chloro- (II; R = Cl, R′ = H, R″ = C_8H_{17}, R‴ = Ac) and 3-acetoxy-4-chloro-1-methyl-19-norcholesta-1 : 3 : 5(10) : 6-tetraene (II; R = H, R′ = Cl, R″ = C_8H_{17}, R‴ = Ac) when heated with toluene-*p*-sulphonic acid and acetic anhydride at 100° or preferably at the boiling point. 2-Chlorocholesta-1 : 4-dien-3-one (V; R = Cl, R′ = H, R″ = C_8H_{17}) was similarly transformed into the "heterophenol," 1-acetoxy-2-chloro-4-methyl-19-norcholesta-1 : 3 : 5(10)-triene [2] (VI; R = C_8H_{17}, R′ = Ac). 4-Chlorocholesta-1 : 4-dien-3-one (V; R = H, R′ = Cl, R″ = C_8H_{17}), in contrast, proved resistant to the "heterophenol rearrangement," even under forcing conditions, a behaviour which accords well with the mechanism of the rearrangement proposed by Woodward and Singh.[3]

Aromatisation of 2- (I; R = Cl, R′ = H, R″ = O·COEt) and 4-chloro-17β-propionoxyandrosta-1 : 4 : 6-trien-3-one (I; R = H, R′ = Cl, R″ = O·COEt) was conveniently effected with toluene-*p*-sulphonic acid in boiling propionic anhydride. Transesterification at position 17 was thereby avoided and the somewhat slow reaction was accelerated. The resultant 6-dehydro-structures (II; R = Cl, R′ = H, R″ = O·COEt, R‴ = COEt; and R = H, R′ = Cl, etc.) were smoothly converted by catalytic hydrogenation into 2- (III;

[1] Part IX, Kirk and Petrow, *J.*, 1958, 1334.
[2] Djerassi and Scholz, *J. Amer. Chem. Soc.*, 1948, **70**, 1911.
[3] Woodward and Singh, *ibid.*, 1950, **72**, 494.

R = Cl, R′ = H, R″ = O·COEt) and 4-chloro-1-methyl-3 : 17β-dipropionoxyœstra-1 : 3 : 5(10)-triene (III; R = H, R′ = Cl, R″ = O·COEt). 2-Chloro-17β-propionoxyandrosta-1 : 4-dien-3-one (V; R = Cl, R′ = H, R″ = O·COEt) yielded 2-chloro-4-methyl-1 : 17β-dipropionoxyœstra-1 : 3 : 5(10)-triene (VI; R = O·COEt. R′ = COEt) which differed from the product (cf. III; R = Cl, R′ = H, R″ = O·COEt) obtained by a normal rearrangement, thus confirming its " heterophenol " character.



Further we prepared 3 : 17β-diacetoxy-1 : 2-dimethylœstra-1 : 3 : 5(10)-triene (III; R = Me, R′ = H, R″ = OAc) from 2α-methyltestosterone acetate[4] (IV; R = H). Dibromination of the latter compound gave the 2β : 6β-dibromo-derivative (IV; R = Br). The β(axial)-configuration of the bromine atoms in this compound seems likely from its method of formation[5] and is supported by the ultraviolet absorption spectrum [$\lambda_{max.}$ (in EtOH) 253 mμ (ε 12,100),[5] (in *cyclo*hexane) 352 mμ (ε 16)[6]] and by the ease with which it passed into 17β-acetoxy-2-methylandrosta-1 : 4 : 6-trien-3-one (I; R = Me, R′ = H, R″ = OAc) on dehydrobromination. Dienone–phenol rearrangement of this trienone furnished the 6-dehydrophenol (II; R = Me, R′ = H, R″ = OAc, R‴ = Ac), which gave 3 : 17β-diacetoxy-1 : 2-dimethylœstra-1 : 3 : 5(10)-triene on catalytic hydrogenation.

The facility with which the foregoing 2-methylated triene undergoes the " dienone–phenol " rearrangement stands in marked contrast to the relative stability of its 2- and 4-chloro-analogues. The electron-attracting chloro-substituents presumably reduce the basicity of the carbonyl-oxygen atom, thus rendering the system less susceptible to attack by the acidic reagent. This is supported by the observed failure of 1 : 2-dichlorocholesta-1 : 4-dien-3-one to undergo the heterophenol rearrangement, even under forcing conditions.[1]

Experimental

Optical rotations refer to chloroform solutions. Ultraviolet absorption spectra were kindly determined by Mr. M. T. Davies, B.Sc.

Dienone–Phenol Rearrangements.—(i) *Of 2-chlorocholesta-1 : 4-dien-3-one* (V; R = Cl, R′ = H, R″ = C_8H_{17}). A mixture of the 2-chlorodienone (1 g.) and toluene-*p*-sulphonic acid (300 mg.) in acetic anhydride (20 ml.) was heated under reflux for 8 hr., then shaken vigorously with water to destroy excess of acetic anhydride, and the steroid was extracted into ether which was washed with sodium hydrogen carbonate solution and water, dried, and evaporated. The resulting gum, dissolved in light petroleum (b. p. 40—60°), was chromatographed on alumina (20 g.). Elution with light petroleum–benzene, followed by crystallisation from methanol, gave *1-acetoxy-2-chloro-4-methyl-19-norcholesta-1 : 3 : 5(10)-triene* (VI; R = C_8H_{17}, R′ = Ac) in needles, m. p. 84—85°, $[\alpha]_D^{22}$ +164° (*c* 0·23), $\lambda_{max.}$ 273 (ε 436) and 281 mμ (ε 404) in ethanol (Found: C, 75·8; H, 9·3; Cl, 7·9. $C_{29}H_{43}O_2Cl$ requires C, 75·9; H, 9·4; Cl, 7·7%).

[4] Ringold and Rosenkranz, *J. Org. Chem.*, 1956, **21**, 1333.
[5] Ellis and Petrow, *J.*, 1956, 1179.
[6] Bird, Cookson, and Dandegaonker, *J.*, 1956, 3675.

(ii) *Of* 2-*chlorocholesta*-1 : 4 : 6-*trien*-3-*one* (I; R = Cl, R′ = H, R″ = C_8H_{17}). The 2-chlorotrienone (0·5 g.) and toluene-*p*-sulphonic acid (0·15 g.) in acetic anhydride (10 ml.) were heated under reflux for 2 hr. The product was isolated and purified as in the previous experiment, giving 3-*acetoxy*-2-*chloro*-1-*methyl*-19-*norcholesta*-1 : 3 : 5(10) : 6-*tetraene* (II; R = Cl, R′ = H, R″ = C_8H_{17}, R‴ = Ac) (130 mg.) in needles, m. p. 80—82°, $[\alpha]_D^{22}$ −108° (*c* 0·19), $\lambda_{max.}$ 226 (ε 27,500), 232 (ε 23,100), 272 mμ (ε = 12,400) in ethanol (Found: C, 75·9; H, 8·9; Cl, 8·0. $C_{29}H_{41}O_2Cl$ requires C, 76·2; H, 8·9; Cl, 7·8%).

(iii) *Of* 4-*chlorocholesta*-1 : 4 : 6-*trien*-3-*one* (I; R = H, R′ = Cl, R″ = C_8H_{17}). A solution of the 4-chlorotrienone (600 mg.) and toluene-*p*-sulphonic acid (100 mg.) in acetic anhydride (15 ml.) was heated under reflux under nitrogen for 8 hr. 3-*Acetoxy*-4-*chloro*-1-*methyl*-19-*norcholesta*-1 : 3 : 5(10) : 6-*tetraene* (II; R = H, R′ = Cl, R″ = C_8H_{17}, R‴ = Ac) separated from the solution on cooling in light brown crystals (540 mg.), m. p. 110—112°. Purified from ethanol it formed prisms, m. p. 119—121°, $[\alpha]_D^{22}$ −129° (*c* 0·31), $\lambda_{max.}$ 227 (ε 28,300), 270·5 mμ (ε = 9·470) in ethanol (Found: C, 76·4; H, 9·0; Cl, 7·5%).

(iv) *Of* 2-*chloro*-17β-*propionoxyandrosta*-1 : 4-*dien*-3-*one* (V; R = Cl, R′ = H, R″ = O·COEt). The 2-chlorodienone (250 mg.) and toluene-*p*-sulphonic acid (50 mg.) in propionic anhydride (5 ml.) were heated at 100° for 40 hr. The brown solution was then shaken with sodium hydrogen carbonate solution to hydrolyse the excess of anhydride, and the product extracted into ether. This solution was washed, dried, and evaporated, and the residue purified from hexane. 2-*Chloro*-4-*methyl*-1 : 17β-*dipropionoxyœstra*-1 : 3 : 5(10)-*triene* (VI; R = O·COEt, R′ = COEt) formed needles, m. p. 114°, $[\alpha]_D^{22}$ +131° (*c* 1·35), $\lambda_{max.}$ 274 mμ (ε 485) in ethanol (Found: C, 69·0; H, 7·7; Cl, 8·1. $C_{25}H_{33}O_4Cl$ requires C, 69·4; H, 7·7; Cl, 8·2%).

(v) *Of* 2-*chloro*-17β-*propionoxyandrosta*-1 : 4 : 6-*trien*-3-*one* (I; R = Cl, R′ = H, R″ = O·COEt). A solution of the 2-chlorotrienone (1·5 g.) and toluene-*p*-sulphonic acid (300 mg.) in propionic anhydride (30 ml.) was heated under reflux for 2·5 hr. The product was isolated as in the previous experiment, and purified from methanol. 2-*Chloro*-1-*methyl*-3 : 17β-*dipropionoxyœstra*-1 : 3 : 5(10) : 6-*tetraene* (II; R = Cl, R′ = H, R″ = O·COEt, R‴ = COEt) formed leaflets (440 mg.), m. p. 127—128°, $[\alpha]_D^{25}$ −131° (*c* 0·39), $\lambda_{max.}$ 226 (ε 29,450), 232 (ε 25,450), and 271 mμ (ε 12,700) in ethanol (Found: C, 70·0; H, 7·5; Cl, 8·1. $C_{25}H_{31}O_4Cl$ requires C, 69·7; H, 7·3; Cl, 8·2%).

The foregoing tetraene (400 mg.) in ethanol (40 ml.) was hydrogenated in the presence of 3% palladium–barium carbonate (10 mg.) at just over 1 atm. until 1 mol. of hydrogen had been absorbed. After filtration from the catalyst and removal of the solvent, purification of the product from methanol gave 2-*chloro*-1-*methylœstradiol dipropionate* (III; R = Cl, R′ = H, R″ = O·COEt) (340 mg.) in needles, m. p. 128—130°, $[\alpha]_D^{21}$ +110° (*c* 0·21), $\lambda_{max.}$ 274 (ε 554) and 282 mμ (ε 550) in ethanol (Found: C, 69·4; H, 7·7; Cl, 8·2. $C_{25}H_{33}O_4Cl$ requires C, 69·3; H, 7·7; Cl, 8·2%).

(vi) *Of* 4-*chloro*-17β-*propionoxyandrosta*-1 : 4 : 6-*trien*-3-*one* (I; R = H, R′ = Cl, R″ = O·COEt). A solution of the trienone (5·5 g.) and toluene-*p*-sulphonic acid (1·5 g.) in propionic anhydride (50 ml.) was heated under reflux for 5 hr., and the product isolated as in previous examples. The crude brown material, in light petroleum–benzene (1 : 1), was percolated through alumina (110 g.), and the resulting colourless oil (3 g.) was purified from methanol. 4-*Chloro*-1-*methyl*-3 : 17β-*dipropionoxyœstra*-1 : 3 : 5(10) : 6-*tetraene* (II; R = H, R′ = Cl, R″ = O·COEt, R‴ = COEt) formed needles (2·2 g.), m. p. 88—89°, $[\alpha]_D^{25}$ −146° (*c* 0·43), $\lambda_{max.}$ 227 (ε 30,800) and 269·5 mμ (ε 9900) in ethanol (Found: C, 69·4; H, 7·4; Cl, 8·6. $C_{25}H_{31}O_4Cl$ requires C, 69·7; H, 7·3; Cl, 8·2%).

4-*Chloro*-1-*methylœstradiol dipropionate* (III; R = H, R′ = Cl, R″ = O·CO·Et).—The 4-chlorotetraene (1 g.) in methanol (50 ml.) was hydrogenated as described for the 2-chlorotetraene. The *product* (450 mg.) separated from hexane in prisms, m. p. 124—125°, $[\alpha]_D^{23}$ +114° (*c* 0·49), $\lambda_{max.}$ 290 (ε 1940), $\lambda_{infl.}$ 285 mμ (ε 1875) in ethanol (Found: C, 69·6; H, 7·7; Cl, 8·0. $C_{25}H_{33}O_4Cl$ requires C, 69·3; H, 7·7; Cl, 8·2%).

17β-*Acetoxy*-2β : 6β-*dibromo*-2α-*methylandrost*-4-*en*-3-*one* (IV; R = Br).—2α-Methyltestosterone acetate (8 g.) in dry ether (500 ml.), cooled in ice, was treated dropwise with bromine in acetic acid (43 ml. of 1·09M-solution). After 15 min., when decolorisation was complete, the ether was removed *in vacuo* without heating. Dropwise addition of water to the residue caused crystallisation of a yellow product, which was purified from methylene chloride–methanol. 17β-*Acetoxy*-2β : 6β-*dibromo*-2α-*methylandrost*-4-*en*-3-*one* formed flakes, m. p. 107—111° (decomp.), $[\alpha]_D^{18}$ −18° (*c* 0·29), $\lambda_{max.}$ 253 mμ (ε 12,100) in ethanol, $\lambda_{max.}$ 352 mμ (ε 16·1) in

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*cyclo*hexane (Found: C, 53·2; H, 5·9; Br, 31·6. $C_{22}H_{30}O_3Br_2$ requires C, 52·6; H, 6·0; Br, 31·8%).

17β-*Acetoxy*-2-*methylandrosta*-1 : 4 : 6-*trien*-3-*one* (I; R = Me, R′ = H, R″ = OAc).—The 2β : 6β-dibromo-compound (8·5 g.) in collidine (60 ml.) was heated under reflux under carbon dioxide for 40 min., collidine hydrobromide (6·2 g., 1·84 mols.) separating. The resulting solution was diluted with ether and washed free from collidine with dilute sulphuric acid. The brown solid remaining after evaporation of the ether was percolated, in benzene, through alumina (30 g.), and purified from methanol. 17β-*Acetoxy*-2-*methylandrosta*-1 : 4 : 6-*trien*-3-*one* formed prisms, m. p. 159—160°, $[\alpha]_D^{19}$ −12° (*c* 0·35), $\lambda_{max.}$ below 220 mμ, 265·5 mμ (ε 11,900), and 300 mμ (ε 10,320) in ethanol (Found: C, 77·6; H, 8·2. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

3 : 17β-*Diacetoxy*-1 : 2-*dimethylæstra*-1 : 3 : 5(10) : 6-*tetraene* (II; R = Me, R′ = H, R″ = OAc, R‴ = Ac).—The 2-methyltrienone (1 g.) in acetic anhydride (20 ml.) containing toluene-*p*-sulphonic acid (300 mg.) was heated at 80° for 4 hr., then poured into water. After extraction with ether and purification from methanol, 3 : 17β-*diacetoxy*-1 : 2-*dimethylæstra*-1 : 3 : 5(10) : 6-*tetraene* formed plates, m. p. 144—146°, $[\alpha]_D^{20}$ −133° (*c* 0·27), $\lambda_{max.}$ 225 (ε 27,950), $\lambda_{infl.}$ 232 (ε 22,000), $\lambda_{max.}$ 268 mμ (ε 11,500) in ethanol (Found: C, 75·0; H, 7·9. $C_{24}H_{30}O_4$ requires C, 75·3; H, 7·9%).

3 : 17β-*Diacetoxy*-1 : 2-*dimethylæstra*-1 : 3 : 5(10)-*triene* (III; R = Me, R′ = H, R″ = Ac).—The 6-dehydro-compound (480 mg.) in ethanol (80 ml.) was hydrogenated in the presence of 2% palladium–barium carbonate (25 mg.) until 1 mol. proportion of hydrogen had been absorbed. 3 : 17β-*Diacetoxy*-1 : 2-*dimethylæstra*-1 : 3 : 5(10)-*triene* separated from methanol in flakes, m. p. 163—164°, $[\alpha]_D^{19}$ +112° (*c* 0·22), $\lambda_{max.}$ 272 (ε = 540) and 280 mμ (ε 530) in ethanol (Found: C, 75·2; H, 8·1. $C_{24}H_{32}O_4$ requires C, 75·0; H, 8·4%).

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159. *Infrared and Nuclear Magnetic Resonance Spectra of Metal–Ethylenediamine Complexes.*

By D. B. POWELL and N. SHEPPARD.

Metal–ethylenediamine * complexes may be divided into two types on the basis of their infrared spectra. It is suggested that these correspond to *gauche* and *cis* configurations of the co-ordinated ethylenediamine molecules. An attempt to confirm the configuration difference by nuclear magnetic resonance spectroscopy was unsuccessful, probably because of mobility of the ring in the *gauche* form.

Infrared Spectra.—Following on previous studies of metal–ammonia complexes [1] it was thought that a spectroscopic investigation of a wide range of ethylenediamine complexes might give interesting comparisons, since the stability of these chelate complexes is generally greater than that of simple ammines and a larger range of metal ions can be investigated.

The infrared spectra of some metal–ethylenediamine complexes have been studied previously, notably the trisethylenediaminecobaltic complex [2] and many *cis–trans* isomers of cobalt(III) and chromium(III) of the type $[Co(en)_2X_2]$,[3] but the variation of the spectra with different metal ions has not been examined in detail. Accordingly we examined the spectra of a number of such complexes from 4000 cm.$^{-1}$ to 400 cm.$^{-1}$; the observed absorption frequencies are listed, weak bands being shown in *italics*, alongside Fig. 1, which shows

* Throughout this paper the symbol (en) is taken to represent a co-ordinated ethylenediamine molecule.

[1] Powell and Sheppard, *J.*, 1956, 3108.
[2] Mizushima and Quagliano, (*a*) *J. Amer. Chem. Soc.*, 1953, **75**, 6084; (*b*) *J. Chem. Phys.*, 1954, **22**, 1614; (*c*) *J. Phys. Chem.*, 1955, **59**, 293.
[3] Merritt and Wiberley, *J. Phys. Chem.*, 1955, **59**, 55.

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the spectra. The compounds were all obtained by standard methods. The octahedral complexes, prepared as hydrates, were heated to 120° to attempt to remove the water of crystallisation; only in the case of the nickel compound was this successful. Many of the complexes have spectra which in overall appearance are similar to that of $[Co(en)_3]^{3+}$, which we term type A spectra, whereas others give a rather simpler pattern of bands (type B spectra). It is clear that the absorption-band patterns of the two types of spectrum differ mainly in three regions, 1400—1250 cm.$^{-1}$, 1200—1000 cm.$^{-1}$, and 650—400 cm.$^{-1}$. The differences are shown most clearly in the octahedral complexes, where the absorption-band patterns for all the compounds having type A spectra are very similar, both in intensities and frequencies, whereas the type B pattern observed for trisethylenediamine-nickel(II) shows marked differences in each of these regions. In particular, in the second region an outstandingly strong band is found for type B spectra at ~1030 cm.$^{-1}$, whereas type A spectra have several absorption bands of comparable intensity. The spectra from 650 cm.$^{-1}$ to 400 cm.$^{-1}$ are sometimes difficult to compare as the presence of water of crystallisation produces a strong broad band in this region.

Discussion of Infrared Spectra.—The very considerable differences between the type A and type B spectra are such as to make it improbable that they are caused by the effect of intermolecular forces between the complex ions. It seems that they must be related to the structure of the complex ions themselves.

Differences of this degree might occur between the spectra of complexes with different overall geometry, for example between octahedral and planar complexes, for such structural changes will cause different amounts of coupling between the vibrations of ligands attached to the same metal ion. However this cannot be the cause of the differences between the two types of spectrum as they are both observed for complexes with similar geometrical arrangements. Thus the octahedral complexes of Co^{III}, Cr^{III}, and Rh^{III} have type A spectra, but that of Ni^{II} is of type B; the planar complexes of Pt^{II} and Pd^{II} {and *trans*-$[Co(en)_2Cl_2]^+$} have type A spectra, whereas the spectrum of the planar $[Cu(en)_2]^{2+}$ ion is of type B. There are however more detailed differences between type A (or type B) spectra of octahedral and planar complexes, undoubtedly due to the different coupling between three and two co-ordinated ethylenediamine molecules respectively.

The only other likely cause of such pronounced spectral differences seems to be a change in configuration of individual co-ordinated ethylenediamine molecules. The likely configurations for such a chelate molecule are *cis* or *gauche* arrangements of the carbon and nitrogen skeleton. Until recently it was generally assumed that such ligands had the *cis* configuration, but definitive *X*-ray diffraction evidence has shown that $[Co(en)_3]Cl_3$ [4] and *trans*-$[Co(en)_2Cl_2]Cl$ [5] are in fact *gauche*. The infrared spectrum of $[Co(en)_3]Cl_3$ supports this conclusion.[2] On this basis the type A spectra, of which that of $[Co(en)_3]Cl_3$ is an example, correspond to *gauche* configuration of the ligand, whereas the type B spectrum may be assumed to correspond to the *cis* form. The higher local symmetry of the latter would account for the simpler spectra.

Although there seems no reasonable alternative explanation of the differences between the two classes of spectrum, an early reference [6] (of which we have only been able to obtain an abstract) refers to the conclusion from *X*-ray studies that in the $[Ni(en)_3]^{2+}$ ion the carbon and nitrogen atoms do not lie in the same plane, and this is one of the complexes which gives a type B spectrum. Our original measurements were made on the chloride, and the *X*-ray work was done on the nitrate, but we have since confirmed that the nitrate has a similar spectrum. There is here a conflict of evidence, which could best be resolved by a detailed *X*-ray diffraction study either of this compound, or of another one of those listed which has a type B spectrum.

[4] (*a*) Nakatsu, Saito, and Kuroya, *Bull. Chem. Soc. Japan*, 1956, **29**, 428; (*b*) Saito, Nakatsu, Shiro, and Kuroya, *Acta Cryst.*, 1955, **8**, 729; (*c*) Nakatsu, Shiro, Saito, and Kuroya, *Bull. Chem. Soc. Japan*, 1957, **30**, 158.

[5] Nakahara, Saito, and Kuroya, *Bull. Chem. Soc. Japan*, 1952, **25**, 331.

[6] Watanabe and Atoji, *Science (Japan)*, 1951, **21**, 301; *Chem. Abs.*, 1951, **45**, 9982 f.

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We intend to publish later a detailed assignment of the spectra to the fundamental vibration frequencies of the complexes.

Nuclear Magnetic Resonance Spectra.—It was considered that the high resolution nuclear magnetic resonance spectra [7] of the complexes with type A and type B infrared spectra might also throw some light on the configurations of the co-ordinated ethylenediamine molecules. A number of those complexes studied by infrared means could not be investigated in this manner, because of either (*a*) limited solubility in water (solid samples do not

FIG. 1. *Infrared spectra of metal–ethylenediamine complexes in the region* 1750—400 *cm.*$^{-1}$ (*Hilger* H800 *spectrometer with* NaCl *and* KBr *prisms*). *The two types of spectrum are designated by* A *and* B. *Broken portions of the curves correspond to hexachlorobutadiene mulls, others to Nujol mulls.*

$[Co(en)_3]Cl_3$ (octahedral hydrate): 3510—3440; 3195—3060; 1619; 1591—1563; 1466; 1366; 1325; *1302*; *1277*; 1251; *1218*; 1163—1155; 1122; 1057; *1002*; *894*; 782; *744*; 523—490—465—435 (Type A).

$[Cr(en)_3]Cl_3$ (octahedral hydrate): 3360; 3190—3060; *2945—2891*; 1620; 1574—1544; 1463; *1394*; 1359; 1330; 1303; *1275*; 1225; 1153—1144; *1115*; 1053; *1005*; *880—869*; 738; 555—530—480—445 (Type A).

$[Rh(en)_3]Cl_3$ (octahedral hydrate): 3528—3440; 3222—3095; 2697—2773; 1620; 1570; 1460; 1364; 1327; 1306; 1279; 1239; 1215; 1165—1156; 1124; 1057; 879; 793; 751; 723; 578—530—506—465 (Type A).

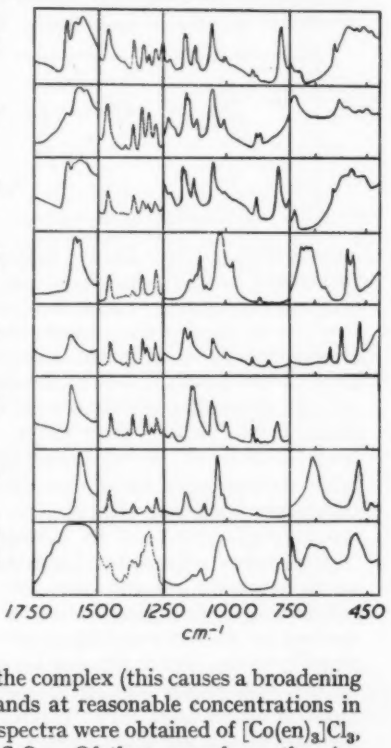
$[Ni(en)_3]Cl_2$ (octahedral): 3480—3400; 3250; 2940—2875; 1587—1569; 1457; *1393*; *1369*; **1330**; **1275**; 1140—1118—1100; *1072*; 1026—974; *865*; 705—683—662; 522—498 (Type B).

$[Pt(en)_2]Cl_2$ (planar): 3207—3141—3064; 1610; 1454; 1373; 1326; 1311; 1275; 1154—1138; 1050; 999; 897; *876*; 831; 589; 546; 478 (Type A).

$[Pd(en)_2]Cl_2$ (planar): 3190—3145—3046; 2960—2875; 1601; 1452; *1390*; 1367; 1317; *1293*; 1273; *1210*; 1134—1125; 1055; *997*; 894; *875*; 798. (Not examined in potassium bromide region) (Type A).

$[Cu(en)_2][PtCl_4]$ (planar): 3562; 3300—3230; 2940—2878; *1633*; 1587; 1459; *1365*; *1315*; 1277; 1162; 1089; 1040—1015; *975*; 700; 550 (Type B).

$[Zn(en)_2][C_2O_4]$ (tetrahedral): *3505—3425*; 3291—3159; *2914—2869*; near 1600 broad band; *1455*; *1398*; 1371; 1303; *1130*; *1100*; 1021; 794—783; 743; 680—625; 500 (spectrum is complicated by presence of strong oxalate bands, but appears to be of type B).



give high resolution spectra), or (*b*) paramagnetism of the complex (this causes a broadening and merging together of the resonance absorption bands at reasonable concentrations in the solution). However, nuclear magnetic resonance spectra were obtained of $[Co(en)_3]Cl_3$, $[Rh(en)_3]Cl_3$, $[Pt(en)_2]Cl_2$, $[Pd(en)_2]Cl_2$, and $[Zn(en)_2]C_2O_4$. Of these complexes the zinc compound gave a very sharp resonance line from the hydrogen atoms of the CH_2 groups, whereas rhodium, palladium, and platinum complexes as a group gave resonance bands of similar shape which were, however, of considerable breadth and had indications of unresolved fine structure (Fig. 2). The latter feature might have been caused by either (*a*) electron-coupled spin–spin interaction between two pairs of non-equivalent hydrogen atoms as might occur with a rigid *gauche* form of the ligand, but not with the *cis* form, (*b*) similar spin–spin interaction between CH_2 and NH_2 groups if the hydrogen atoms of the latter do not exchange sufficiently rapidly with those of the water solvent, or (*c*) a combination of these two effects.

The presence of effect (*b*) can be readily checked by dissolving the substance in D_2O and thereby replacing the hydrogen atoms of the NH_2 groups by deuterium. Because of

[7] Wertz, *Chem. Rev.*, 1955, **55**, 829.

the different magnetic moment and spin of the latter nucleus any interaction of the ND_2 groups with the CH_2 hydrogen atoms is expected to be much smaller. In fact in all cases except the cobalt complex, replacement of the NH_2 groups by ND_2 caused the broad resonances to become sharp lines as in the case of the zinc compound, showing that effect (*b*) was the only operative one. With the cobaltic complex a rather broader resonance band was originally observed for the CH_2 groups, presumably owing to the presence of extra structure caused by interaction with the magnetic moment of the cobalt nucleus of spin $\frac{7}{2}$; as expected some line-breadth persisted in the spectrum of the deutero-compound.

The fact that each of the CH_2 resonances consists of a sharp line after elimination of the effect due to NH_2 hydrogen atoms shows that all the four methylene hydrogen atoms are effectively chemically equivalent. This would be expected for the *cis* configuration of the

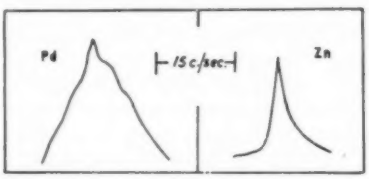


FIG. 2. *Nuclear magnetic resonance spectra of the hydrogen nuclei of* CH_2 *groups in the ethylenediamine complexes* $[Pd(en)_2]Cl_2$ *and* $[Zn(en)_2]C_2O_4$ *scanned at the same rate (Varian Associates* 4300 B *spectrometer); the spectra are slightly asymmetrical owing to inclusion of a small amount of dispersion with the absorption mode.*

co-ordinated ethylenediamine molecule which has a plane of symmetry through the two carbon and two nitrogen atoms. In the case of a fixed *gauche* configuration, the plane of symmetry is destroyed and the two-fold axis through the centre of the carbon–carbon bond causes the hydrogen atoms to be structurally equivalent only in two separate pairs. However, if the co-ordinated molecule can change with sufficient rapidity from one *gauche* form to the equivalent form obtained by movement of the carbon and nitrogen atoms through the median plane, then the plane of symmetry is effectively restored. As a likely chemical shift between the two non-equivalent pairs of hydrogen atoms of the *gauche* form is about 10 c./sec., the simplified spectra will be observed if the *gauche* forms are being interconverted with about this order of magnitude of frequency. This is probably why the nuclear magnetic resonance spectra do not allow a distinction to be made between the configurations suggested by infrared means.

Conclusion.—The infrared spectra provide a criterion for dividing the metal–ethylenediamine complexes into two types, and it is suggested that these correspond to the alternative *gauche* and *cis* configurations of the ligand. Attempts to confirm these structural conclusions by nuclear magnetic resonance spectra were unsuccessful, probably owing to the mobility of the ring in the *gauche* configuration.

It is noteworthy that, of the complexes studied, those with type A spectra, *i.e.*, with *gauche* configurations, are more stable than those with type B spectra, although as yet too few have been investigated to make a reliable generalisation on this point. Also, we noted during the nuclear magnetic resonance experiments that the hydrogen atoms of NH_2 groups of co-ordinated ethylenediamine molecules exchange with deuterium in D_2O solutions at very different rates. Thus, with $[Pt(en)_2]Cl_2$ the exchange took about 12 hr. to go to completion, whereas with $[Rh(en)_3]Cl_3$ the exchange took about 30 min. The lack of observation of structure on the CH_2 resonances of $[Zn(en)_2]C_2O_4$ implies that in this case the NH_2 hydrogen atoms of the ligand exchange at a rate probably exceeding 100 $sec.^{-1}$, *i.e.*, $2\pi\Delta\nu$, where $\Delta\nu$ ($\sim$15 c./sec.) is a typical half-width of a band with structure due to spin–spin coupling of CH_2 and NH_2 groups (see Fig. 2).

Another interesting difference between the spectra of the platinum and rhodium complexes is that whereas the ^{195}Pt nucleus (spin $\frac{1}{2}$, natural abundance 34%) causes an extra pair of bands in the spectrum of the CH_2 group centred about the main resonance with the surprisingly large spin–spin splitting of $\sim$45 c./sec., the abundant ^{103}Rh nucleus (also with spin $\frac{1}{2}$) does not appear to cause an observable splitting of the CH_2 resonance. Under the

experimental conditions such a splitting must be less than 3 c./sec. Thus the Pt–H coupling constant is at least 15 times greater than the corresponding Rh–H constant, although the magnetogyric ratio of the ^{195}Pt nucleus is only 6 times that of ^{103}Rh. This implies that the intervening electron distributions couple together the platinum and hydrogen nuclei more effectively than rhodium and hydrogen.

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160. *An Investigation of the "Ziegler" Catalysts obtained by treating Titanium Tetrachloride with Aluminium Alkyls.*

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An investigation of the catalytic materials obtained by treating titanium tetrachloride in petrol solution with aluminium alkyls is described. All products were isolated and analysed, attention being concentrated on the dark solids formed on mixing the reactants. Examination of these solids indicated that they were complexes of organo-aluminium compounds with the lower titanium chlorides. Reduction of $TiCl_4$ by AlR_3 is accompanied by the production of hydrocarbons, and a relationship was established between the volume of RH evolved and the degree to which the $TiCl_4$ was reduced. This was consistent with the liberation of free alkyl radicals, R·, which disproportionate when R is Et, Pr^n, or Bu^n, and abstract hydrogen from the solvent when R is Me. The structure of the complexes and the mechanism by which they catalyse the polymerisation of olefins are discussed.

MANY references to the reaction between aluminium alkyls and titanium halides have appeared since Ziegler's discovery[1] that the brown or black solid product is an active catalyst for the polymerisation of ethylene at low pressures. It is generally agreed that these solids, which are insoluble in hydrocarbons,[2–4] are formed by reduction of titanium tetrachloride,[3,5,6] and the evolution of hydrocarbon gases, a necessary consequence of reduction by the alkyl, has been observed.[7] The evolution of ethane and ethylene, which can arise from the disproportionation of ethyl radicals, has been detected during the reaction between $AlEt_3$ and $TiCl_4$,[8] but no quantitative measurements were made. Other workers[9] have assumed that the alkyl radicals liberated during reduction react only by abstracting hydrogen from the solvent. It has been stated[7] that very little reduction beyond tervalent titanium occurs during the preparation of active catalysts from $AlBu^i_3$ and $TiCl_4$, but several patents[5,10] claim that the presence of bivalent titanium is essential for catalytic activity. Solids obtained from titanium tetrachloride and triethylaluminium contain Cl, Al, Ti, and ethyl groups, and it has been shown[8] that as the ratio $AlEt_3 : TiCl_4$ is increased the ratio Cl : Ti in the solids decreases, while the ratio Al : Ti increases. However, no complete analysis of these solids has been reported. In the present work

[1] Ziegler, *Angew. Chem.*, 1955, **67**, 541.
[2] Belgian Patent 546,846.
[3] Belgian Patent 545,087.
[4] Italian Patent 537,425.
[5] Italian Patent 549,915.
[6] Belgian Patent 540,459.
[7] Friedlander and Oita, *Ind. Eng. Chem.*, 1957, **49**, 1885.
[8] Longi, Mazzanti, Natta, and Pino, *Gazzetta*, 1957, **87**, 549.
[9] Anderson, Ashby, and Ludlum, *J. Amer. Chem. Soc.*, 1958, **80**, 1380.
[10] U.S.P. 2,721,189.

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a quantitative study of the reaction has been attempted, in which all the products have been isolated and completely analysed.

Experimental

Materials.—Solvents were all sodium-dried analytical-reagent quality light petroleums, which were free from aromatic hydrocarbons. $AlMe_3$ (Found: Al, 37·5; C, 49·9; H, 12·5. Calc. for AlC_3H_9: Al, 37·5; C, 50·0; H, 12·5%), $AlPr^n_3$ (Found: Al, 17·5; C, 68·1; H, 13·4. Calc. for AlC_9H_{21}: Al, 17·3; C, 69·2; H, 13·6%), and $AlBu^n_3$ (Found: Al, 13·5; C, 69·2; H, 13·1. Calc. for $AlC_{12}H_{27}$: Al, 13·65; C, 72·7; H, 13·65%) were prepared by standard methods and diluted with light petroleum before use. $AlEt_3$ was obtained in methyl*cyclo*hexane solution and was not therefore analysed. The concentrations of aluminium alkyl in the solutions used were determined by analysing these solutions for aluminium.

Reaction between Titanium Tetrachloride and Aluminium Alkyls at 20°.—(1) *Procedure.* Aluminium alkyls (0·0125—0·25 mole), dissolved in light petroleum (b. p. 100—120°), were added to stirred solutions of $TiCl_4$ (0·0125—0·05 mole), the total volume of solvent being 400 ml. When the alkyl was $AlEt_3$, $AlPr^n_3$, or $AlBu^n_3$ brown (low $[AlR_3]$ used) or black (high $[AlR_3]$ used) precipitates were formed immediately, but with $AlMe_3$ precipitation was so slow that the reaction could not conveniently be investigated at 20°. $AlEt_2Cl$ gave a precipitate with $TiCl_4$ less rapidly than $AlEt_3$, and $AlEtCl_2$ was still less reactive. After being stirred for 2 hr., the products were filtered, and the solid residues washed several times with light petroleum (b. p. 40—60°). All the above operations were carried out under nitrogen, air being rigorously excluded.

(2) *The solids.* Solvent was removed by drying, first under low vacuum (10^{-1} mm.), and then to constant weight under high vacuum (10^{-3} mm.). During the latter process, which took 48 hr., the solids lost *ca.* 10% of their weight, the material removed being trapped and then shown to be solvent by its infrared spectrum. When ethylene was passed through a suspension of the dried solid, obtained from $AlEt_3$ (0·02 mole) and $TiCl_4$ (0·025 mole), in light petroleum for 1·5 hr., 15 g. of solid polymer were obtained. The same weight of polymer was obtained when the experiment was repeated with use of a similar solid catalyst which had been washed and

Table 1. *Analysis of solids prepared at* 20°.

	Reactants			Composition of the solids				
				Atomic or group ratios of:				Polymer:
Expt. No.	Moles $TiCl_4$ (moles)	Alkyl (moles)	Alkyl	Al : Ti	Cl : Ti	Alk : Ti	Alk : Al	(C + H) as wt. %
1	0·025	0·02	$AlEt_3$	0·152	3·18	0·26	1·7	38
2	0·025	0·02	,,	0·159	3·26	0·20	1·3	41
40	0·025	0·025	,,	0·27	3·17	0·37	1·4	25
3	0·025	0·0375	,,	0·46	2·99	1·03	2·3	23
4	0·025	0·0375	,,	0·41	3·06	0·77	1·9	27
5	0·025	0·05	,,	0·58	2·78	1·19	2·0	20
6	0·025	0·05	,,	0·57	2·97	0·95	1·8	22
7	0·025	0·075	,,	0·41	1·88	1·41	3·4(?)	22
8	0·025	0·125	,,	0·42	1·82	1·31	3·1	21
9	0·025	0·25	,,	0·55	1·51	1·21	2·2	27
15	0·025	0·0075	$AlPr^n_3$	0·18	3·31	0·14	0·8	41
16	0·025	0·0125	,,	0·14	3·21	0·17	1·2	25
17	0·025	0·02	,,	0·12	3·13	0·16	1·3	7
10	0·05	0·05	,,	0·21	3·07	0·45	2·2	12
18	0·025	0·0375	,,	0·25	2·84	0·62	2·5	7
11	0·05	0·10	,,	0·49	2·42	1·27	2·6	8
12	0·05	0·15	,,	0·45	1·75	1·09	2·5	10
13	0·05	0·25	,,	0·37	1·35	0·96	2·6	18
14	0·025	0·25	,,	0·37	1·19	0·87	2·4	21
31	0·025	0·0125	$AlBu^n_3$	0·18	3·25	0·19	1·1	6
32	0·0125	0·0125	,,	0·15	2·98	0·25	1·7	11
33	0·0125	0·025	,,	0·34	2·49	0·81	2·4	2
34	0·0125	0·0375	,,	0·43	1·88	0·96	2·2	4
27	0·025	0·0375	$AlEt_2Cl$	0·14	3·20	0·34	2·4(?)	23
28	0·025	0·1125	,,	0·20	3·21	0·38	1·9	31
29	0·0125	0·0938	,,	0·29	3·14	0·26	0·9	53
30	0·0125	0·1875	,,	0·28	3·33	0·33	1·2	39

filtered off, but not dried. As the dried solids were very rapidly oxidised by air (many inflamed spontaneously) the weighed samples required for analysis, etc., were dispensed and then handled completely under nitrogen. The extent of oxidation by adventitious air was apparent from the difference between the total analysis and 100%; the figures quoted in the subsequent tables are based on analyses for which the sum C + H + Cl + Al + Ti% was generally ≥98%.

Weighed samples of the solids were examined as follows. (*a*) Microcombustion for carbon and hydrogen. (*b*) Hydrolysis with dilute sulphuric acid in a closed flask (to prevent the loss of halogen); the product was filtered to give a waxy residue, which was dried and weighed, and a solution which was analysed for Al, Ti, and Cl by standard methods. The nature of the waxy residue was established as follows. A mixture of dilute hydrochloric acid and methanol was added to the solid obtained by treating $TiCl_4$ (0·050 mole) with $AlEt_3$ (0·15 mole), and the wax obtained was filtered off, washed, and dried. The infrared spectrum of this solid showed that it was 98% polyethylene. A similar experiment carried out with the solid obtained from $TiCl_4$ and $AlPr^n_3$ gave polypropene as the principal solid product. (*c*) The gaseous hydrolysis products were examined by transferring a weighed sample to a flask fitted with a manometer, which was then evacuated. Dilute sulphuric acid (10 ml.) and a wetting agent were introduced and the pressure produced by gas evolution was measured. The volume of gas evolved at N.T.P. was calculated from the known volume of the flask and the pressure developed, and the composition of the gas measured by comparing its infrared spectrum with those of standard samples of the hydrocarbons known to be present. Hydrogen was determined by gas chromatography. (*d*) The solid obtained from $TiCl_4$ (0·05 mole) and $AlPr^n_3$ (0·15 mole) was heated in a

TABLE 2. *Decomposition of solids obtained from* $AlPr^n_3$ *and* $TiCl_4$ *with dilute sulphuric acid.*

Catalyst preparation Expt.	Al : Ti reactant ratio	C in solid (%)	H in solid (%)	H per C_3	% of total carbon appearing as (*a*) C_3H_8	(*b*) C_3H_6	(*c*) $(C_3H_6)_n$	$a + b + c$	CH_4	Moles of H_2 evolved [a] per mole of Ti present
10	1·0	9·8	2·0	7	74·6	1·8	11·9	88·3	0·0	0·008
11	2·0	22·4	6·4	10	59·4	11·5	8·3	79·2	1·2	0·052
					65·5	8·3		84·1	2·4	0·055
12	3·0	24·8	4·4	6	45·4	22·1	8·9	76·4	8·6	0·493
					43·9	30·2		83·1	7·4	0·565
13	5·0	25·6	5·2	7	73·3	4·4	18·2	95·9	6·8	0·700
					75·6	5·0		98·0	5·1	0·694
14	10·0	25·9	4·7	7	40·0	16·2	20·6	76·8	10·8	0·716

TABLE 3. *Analysis of filtrates from reactions between* $TiCl_4$ *and* $AlEt_3$ *at 20°.*

Expt.	Al : Ti ratio of reactants	% of reactant appearing in filtrate Al	Cl	Ti	Colour of filtrate	Expt.	Al : Ti ratio of reactants	% of reactant appearing in filtrate Al	Cl	Ti	Colour of filtrate
1	0·8	82	18	0·8	Light brown	5	2·0	70	34	3·2	Black
2	0·8	82	20	1·2		6	2·0	79	23	3·3	
3	1·5	87	16	8·7	Brown	7	3·0	85	53	3·3	
4	1·5	70	16	1·7		8	5·0	92	51	11	
						9	10·0	95	49	26	

sealed evacuated tube to 400° for 16 hr. A small quantity (*ca.* 0·1 ml.) of liquid was collected in a side tube cooled in liquid air. This vaporised when warmed to room temperature and an analysis of the gas remaining in the tube showed only a trace of methane.

(3) *Numerical results.* The results of analyses carried out as described in sections 2(*a*) and 2(*b*) are given in Table 1. In calculating these data, the percentage of carbon and hydrogen present in the solids as alkyl groups was assumed to be the difference between the percentage of carbon and hydrogen found by microcombustion, and that of polymer isolated on hydrolysis; the alkyl ratios were therefore calculated from the percentage of carbon in the solids that did not appear as polymer on hydrolysis. This assumption is reasonable, for the H : C ratios in the solids were found to be close to those of the appropriate alkyl groups (see, *e.g.*, Table 2), and in the case of the solids obtained from $AlPr^n_3$ and $TiCl_4$ a high proportion of the volatile organic hydrolysis products [isolated as described in section 2(*c*)] were propane and propene (Table 2).

(4) *Filtrates.* Filtrates from reactions between $TiCl_4$ and $AlEt_3$ were treated with dilute sulphuric acid, and the aqueous extract analysed for Al, Cl, and Ti by standard methods (see Table 3). The black filtrates did not give precipitates on standing, but when they were centrifuged in closed tubes at 11,000 r.p., a black solid separated out, leaving the liquid clear and almost colourless. Thus it appears that the soluble products are not deeply coloured, the intense colour and the titanium content of some filtrates being due to finely divided solids that

TABLE 4. *Alkyls present in the filtrates from reactions between* AlR_3 *and* $TiCl_4$ *at* 20°.

Expt.	Alkyl	Al : Ti reactant ratio	Compn. of filtrate: ratios Cl : Al	Alk : Al	Expt.	Alkyl	Al : Ti reactant ratio	Compn. of filtrate: ratios Cl : Al	Alk : Al
1	$AlEt_3$	0·8	1·25	1·75	11	$AlPr^n_3$	2·0	1·05	1·95
17	$AlPr^n_3$	0·8	1·30	1·70	33	$AlBu^n_3$	2·0	0·90	2·10
40	$AlEt_3$	1·0	0·93	2·07	7	$AlEt_3$	3·0	0·83	2·17
10	$AlPr^n_3$	1·0	1·18	1·82	12	$AlPr^n_3$	3·0	0·88	2·12
32	$AlBu^n_3$	1·0	1·20	1·80	34	$AlBu^n_3$	3·0	0·80	2·20
3	$AlEt_3$	1·5	0·61	2·39	8	$AlEt_3$	5·0	0·46	2·54
18	$AlPr^n_3$	1·5	0·90	2·10	13	$AlPr^n_3$	5·0	0·57	2·43
6	$AlEt_3$	2·0	0·58	2·42	9	$AlEt_3$	10·0	0·21	2·79
					14	$AlPr^n_3$	10·0	0·27	2·71

had passed through the filter. Ethylene was passed through several of the filtrates for 0·5 hr., but no absorption occurred and no polymer separated on addition of methanol. Filtrates from reactions between $TiCl_4$ and AlR_3, where R = Et or Pr-, were treated with a few c.c. of methanol, filtered, evaporated to dryness, and the solids retained. Examination of their infrared absorption spectra showed them to be polyethylene when R = Et and polypropene when R = Pr^n.

The ratios of Cl : Al in the filtrates, and the Alk : Al ratios calculated from them, are recorded in Table 4; the values obtained when the alkyl was $AlEt_3$ were determined as described above, and those for the other alkyls by calculation from the compositions of the corresponding solids, it being assumed that the filtrates did not contain significant amounts of $TiCl_4$. In the last four experiments it is also assumed that the composition of the solid passing through the filter is not much different from that which the filter retains.

TABLE 5. *Analysis of solids prepared at* ca. 100°.

Expt. No.	Reactants $TiCl_4$ (moles)	Alkyl (moles)	Alkyl	Composition of the solids: Atomic or group ratios of Al : Ti	Cl : Ti	Alk : Ti	Alk : Al	Polymer: (C + H) as wt. %
41	0·025	0·025	$AlMe_3$	0·077	2·70	0·20	2·6	36
42	0·025	0·0375	,,	0·22	2·81	0·57	2·6	8
43	0·025	0·050	,,	0·33	2·41	0·93	2·8	11
44	0·025	0·075	,,	0·56	1·54	1·83	3·3	*
36	0·05	0·04	$AlEt_3$	0·19	3·28	0·15	0·8	22
37	0·05	0·075	,,	0·20	2·77	0·42	2·1	36
38	0·025	0·05	,,	0·40	2·36	0·62	1·6	18
39	0·05	0·15	,,	0·56	1·69	1·02	1·8	16
19	0·025	0·0075	$AlPr^n_3$	0·14	3·22	0·15	1·1	22
20	0·025	0·0125	,,	0·16	3·32	0·07	0·4	36
21	0·05	0·04	,,	0·15	3·06	0·18	1·2	6
22	0·05	0·075	,,	0·33	2·84	0·45	1·3	5
23	0·05	0·10	,,	0·29	2·51	0·49	1·7	3
24	0·025	0·075	,,	0·39	1·82	0·76	2·0	4
25	0·025	0·125	,,	0·36	0·82	0·55	1·0	13
26	0·025	0·25	,,	1·51	0·14	0·82	0·5	6

* Not measured.

Reaction between Titanium Tetrachloride and Aluminium Alkyls at ca. 100°.—It was suspected that gaseous hydrocarbons were produced during the reaction at 20°, but that they dissolved in the solvent. Solutions of titanium tetrachloride in boiling light petroleum (b. p. 100—120°) were therefore treated under reflux with aluminium alkyl solutions, and the gases which boiled off through the condenser were collected. The volume of gas evolved at N.T.P. was determined, and the composition of the gas measured by infrared spectroscopy. Isolation and analysis of

the solid products were carried out as previously described. When the alkyl was $AlMe_3$ the gases evolved were methane (80—90%) and ethylene (10—20%), while with $AlEt_3$, ethane (94 ± 2%) and ethylene (6 ± 2%) were obtained. $AlPr^n_3$ gave propane and propene, the proportion of the latter rising from 10 to 35% as the Alkyl : $TiCl_4$ ratio was increased from 0·5 to 5·0 : 1. When ethylene was passed through the total reaction products rapid absorption occurred and solid polymers were obtained.

Discussion

It appears that the Ziegler catalyst's activity is associated with its insoluble solid component, the composition of which depends upon its preparation. The average valency of titanium in the solids (Table 6), calculated from the analytical data on the assumption that the Al, Cl, and alkyl radicals all exert their normal covalencies, ranges from 3 to <1, the extent to which $TiCl_4$ is reduced depending largely on the amount of $AlAlk_3$ used. Bivalent titanium reacts with acids to give hydrogen,[11] so that the formation of hydrogen on hydrolysis of the solids (see Table 2) confirms the presence of titanium in a valency state lower than 3. With the exception of $AlMe_3$, all the trialkyls investigated appear to have roughly the same power to reduce $TiCl_4$, but the dialkyl chloride, $AlEt_2Cl$, was less reactive and did not reduce the valency of titanium much below 3. The ratio Alk : Al in the filtrate from reactions between $TiCl_4$ and $AlAlk_3$ investigated at 20° (Table 4) ranged from 1·7 to 2·8, so that the dialkyl chlorides can play only a small part in the reduction.

Results from the reactions at 100° show that there is usually close agreement between the valency of titanium in the solid calculated from the analytical results (col. A, Table 7) and that deduced from the volume of alkane (col. B) on the assumption that ½ mole of alkane is produced for every unit reduction of a titanium g.-atom. Thus the alkyl groups, R, liberated on reduction disproportionate as follows: $2R \longrightarrow R(-H) + R(+H)$, when R is Et, Pr^n, or Bu^n. However, the relative proportions in which alkene and alkane were evolved were always less than 1 : 1 because much of the alkene polymerised, the polymer appearing in both the solids and the filtrates. Ethylene is polymerised by Ziegler catalysts more readily than propene, so that the alkene to alkane ratio obtained when $TiCl_4$ was

Table 6. *Valency of titanium in the solids obtained at* 20°.

Expt. No.	Alkyl	Al : Ti ratio	Average Ti valency in solid	Expt. No.	Alkyl	Al : Ti ratio	Average Ti valency in solid
15	$AlPr^n_3$	0·3	2·91	7	$AlEt_3$	3·0	2·04
16	$AlPr^n_3$	0·5	2·96	12	$AlPr^n_3$	3·0	1·49
17	$AlPr^n_3$	0·8	2·93	34	$AlBu^n_3$	3·0	1·55
40	$AlEt_3$	1·0	2·83	28	$AlEt_2Cl$	*3·0	2·99
10	$AlPr^n_3$	1·0	2·89	8	$AlEt_3$	5·0	1·87
32	$AlBu^n_3$	1·0	2·78	13	$AlPr^n_3$	5·0	1·20
27	$AlEt_2Cl$	*1·0	3·12	29	$AlEt_2Cl$	*5·0	2·53
6	$AlEt_3$	2·0	2·31	9	$AlEt_3$	10·0	1·07
11	$AlPr^n_3$	2·0	2·22	14	$AlPr^n_3$	10·0	0·95
33	$AlBu^n_3$	2·0	2·28	30	$AlEt_2Cl$	*10·0	2·82

* The Al : Ti ratio quoted is two-thirds of that used, so that the ratios quoted for $AlEt_2Cl$ are comparable with those quoted for AlR_3.

treated with $AlPr^n_3$ was, as expected, greater than when $AlEt_3$ was used. The above correlation, between the valency of titanium in the solid and the volume of alkane evolved, was not obtained with $AlMe_3$, considerably more methane being produced than would be expected if quantitative disproportionation of the liberated methyl groups had occurred. Thus it appears that the alkyl groups are liberated as free radicals, for it is known [12] that the Et, Pr^n, and Bu^n free radicals disproportionate in solution, while free methyl radicals react principally by abstracting hydrogen from the solvent.

The valency of titanium calculated for the solids obtained in Expts. 25 and 26 (Table 7)

[11] Sidgwick, "The Chemical Elements and their Compounds," O.U.P., Oxford, 1950, p. 651.
[12] Kharasch and Reinmuth, "Grignard reactions of non-metallic substances," Constable and Co. Ltd., London, 1954, p. 124.

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TABLE 7. *Reduction of titanium tetrachloride by aluminium alkyls at* 100°.

Expt.	Alkyl	Al : Ti ratio	Valency of Ti in solid A	Valency of Ti in solid B	Expt.	Alkyl	Al : Ti ratio	Valency of Ti in sold A	Valency of Ti in sold B
20	$AlPr^n_3$	0·5	2·91	3·13	38	$AlEt_3$	2·0	1·78	1·80
36	$AlEt_3$	0·8	2·86	2·98	23	$AlPr^n_3$	2·0	2·13	2·36
21	$AlPr^n_3$	0·8	2·79	3·06	44	$AlMe_3$	3·0	1·69	−0·67
41	$AlMe_3$	1·0	2·67	2·48	39	$AlEt_3$	3·0	1·03	0·77
42	$AlMe_3$	1·5	2·72	1·97	24	$AlPr^n_3$	3·0	1·41	1·42
37	$AlEt_3$	1·5	2·69	2·48	25	$AlPr^n_3$	5·1	0·29	−1·36
22	$AlPr^n_3$	1·5	2·30	2·34	26	$AlPr^n_3$	10·0	−3·57	−6·4
43	$AlMe_3$	2·0	2·35	1·04					

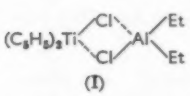
is not reasonable, and indicates that these solids contain metallic (and not tervalent) aluminium. The metal could be formed by reactions such as

$$Al(CH_3{\cdot}CH_2{\cdot}CH_2)_3 \longrightarrow AlH(CH_3{\cdot}CH_2{\cdot}CH_2)_2 + CH_3{\cdot}CH{:}CH_2$$
$$AlH(CH_3{\cdot}CH_2{\cdot}CH_2)_2 \longrightarrow Al + 1\tfrac{1}{2}H_2 + 2CH_3{\cdot}CH{:}CH_2$$

which are known [13a,14] to occur during the pyrolysis of aluminium alkyls, and it is significant that anomalous values were not obtained for the valency of titanium in similar experiments performed at 20° (Expts. 13 and 14 in Table 6).

It has been suggested [7,8] that the reduction of $TiCl_4$ by $AlAlk_3$ proceeds *via* alkyltitanium halides, *e.g.*, $TiCl_3Alk$, $TiCl_2Alk_2$, which decompose to give lower titanium halides and alkyl radicals. These intermediates would certainly be unstable, for all attempts made to isolate titanium alkyls [15] failed. However, aluminium alkyls readily form co-ordination compounds, *e.g.*, $Me_3\bar{A}l{\cdot}\overset{+}{N}Me_3$ and $K^+Al\bar{E}t_3F$,[13b] with electron donors, so that the first step in their reaction with $TiCl_4$ may well be the formation of complexes such as $Cl_3Ti\overset{+}{\bar{C}l}{\cdot}\bar{A}lAlk_3$ or $Cl_2Ti(\overset{+}{\bar{C}l}\bar{A}lAlk_3)_2$. These could then decompose directly by homolytic fission of the appropriate Ti–Cl and Al–Alk bonds. Monomeric alkyls are required for the formation of these complexes, so that, in agreement with our experiments, those alkyls which form particularly stable dimers, *e.g.*, $AlMe_3$,[13c] $AlAlk_2Cl$,[13d] would not be expected to react as readily as the higher trialkyls whose dimers are more readily dissociated.

The catalytic solids always contain Ti, Al, and alkyl groups, but there is, as yet, no direct evidence indicating to which metal atom the alkyl groups are attached. Thus there are two main theories concerning these catalysts: (*a*) They contain titanium alkyls, *e.g.*, $TiCl_3Alk$, and olefin polymerisation occurs at the reactive Ti–Alk bonds.[16,9] (*b*) They are mixtures or complexes of the lower titanium halides with aluminium alkyls (or chloroalkyls) and polymerisation occurs by addition of olefin molecules to the Al–Alk bonds.[16] End-group analysis of polymers produced with selected catalysts [16] has provided some support for the second alternative. Our results show that the solids cannot contain significant quantities of $AlCl_3$, for the dialkyl chlorides play little part in the reduction of $TiCl_4$ and the alkyl dichlorides react even less readily. They also indicate the absence of highly unstable bonds, for the activity of the solids was not reduced by high-vacuum drying. Further, although the ratio Alk : Ti, in the solids varied by a factor of 10, the Alk : Al ratio was usually between 1 and 3 (see Table 1). These data are consistent with the second theory, while the failure to obtain aluminium alkyls from the solids either by vacuum drying or by pyrolysis shows that the alkyls are chemically bound, rather than absorbed physically, to the titanium halides. Natta and his co-workers [17] have recently prepared a blue complex, to which the bridge structure, (I)



(I)

[13] Coates, "Organo-metallic Compounds," Methuen and Co. Ltd., London, 1956, (*a*) p. 72; (*b*) p. 79; (*c*) p. 75; (*d*) p. 82.
[14] Lecture given by Schultz, of the Hercules Powder Corporation, at Massachusetts, U.S.A., July, 1956.
[15] *E.g.*, Gilman and Jones, *J. Org. Chem.*, 1954, **10**, 505.
[16] Giannini, Mantica, Mazzanti, Natta, Peraldo, and Pino, *Chimica e Industria*, 1957, **39**, 19.
[17] *Idem*, *J. Amer. Chem. Soc.*, 1957, **79**, 2975.

has been attributed, by treating di(*cyclo*pentadienyl)titanium dichloride with $AlEt_3$. However, this complex appears to be very different from the insoluble infusible solids under investigation, for it is soluble in hydrocarbons, melts at 126—130°, and is far less active as a polymerisation catalyst.[17] Further, only the expected gaseous hydrocarbon, ethane, was evolved when the complex (I) was treated with water,[17] whereas the solids obtained by treating $TiCl_4$ with $AlPr^n_3$ gave propane, propene, methane, and hydrogen on hydrolysis. Thus it appears that Natta's complex is not a good analogy for the Ziegler catalyst.

Solids obtained from $TiCl_4$ and $AlEt_3$ give *X*-ray diffraction patterns resembling that of $TiCl_3$ and it has been suggested that they contain layers of titanium atoms similar to those in $TiCl_3$ (or $TiCl_2$ which also has a layer lattice structure [18]), although the arrangement of the layers relative to one another may be different.[19] Thus it is possible that the solids have layer structures similar in nature to those of the lower titanium halides, in which the chlorine layers are modified by partial replacement of chlorine ions with anions such as $\bar{Al}ClEt_3$, $\bar{Al}Cl_2Et_2$, or $\bar{Al}Cl_3Et$, these anions being formed by the co-ordination of $AlEt_3$, $AlEt_2Cl$, or $AlEtCl_2$ with chlorine ions already present in the lattice. This type of structure is consistent with both the physical properties and the chemical composition of the solids. The formation of propene and methane as well as propane during the hydrolysis of solids obtained from $AlPr^n_3$ and $TiCl_4$ appears to be connected with the presence of titanium in a valency state below 3 (compare Tables 2 and 6). Solids in which the average valency of titanium was well below 3 also gave considerable quantities of hydrogen on hydrolysis (Table 2), and it is possible that the hydrogen atoms first produced, which normally combine to give hydrogen molecules, also react with the anions:

$$Ti^{3+} + H_2O \longrightarrow Ti^{3+} + OH^- + H$$
$$2H \longrightarrow H_2$$
$$H + \bar{Al}(C_3H_7)_3Cl \longrightarrow H\bar{Al}(C_3H_7)_2Cl + C_3H_7$$

Propene and methane could both be formed in such a system; the former by disproportionation of propyl radicals, and the latter *via* the series of reactions postulated by Steacie [20] to explain the formation of methane in gaseous systems containing hydrogen atoms and propyl radicals at temperatures below 100°:

$$2C_3H_7 \longrightarrow C_3H_6 + C_3H_8$$
$$C_3H_7 + H \longrightarrow C_2H_5 + CH_3$$
$$C_2H_5 + H \longrightarrow 2CH_3$$
$$CH_3 + H \longrightarrow CH_4$$

Propane would also be formed by direct hydrolysis of the complex anions.

Initiation of olefin polymerisations, catalysed by the lattice structure suggested above, is more likely to occur at the titanium atoms than at the complex anions, for complexes formed from aluminium alkyls and electron donors react less readily with ethylene than do the alkyls themselves [21] and the catalytic activity of the solid is much greater than that of aluminium alkyls. Further, titanium dichloride is, by itself, a catalyst for ethylene polymerisations,[22] and in this case titanium atoms appear to be the only sites available for initiation. It is therefore suggested that ethylene molecules become

[18] Wells, "Structural Inorganic Chemistry," Clarendon Press, Oxford, 1950, p. 278.
[19] Howells, personal communication.
[20] "Atomic and Free Radical Reactions," Reinhold Publishing Corp., New York, 1954, p. 468.
[21] Ziegler, "Perspectives in Organic Chemistry" (Ed. by Todd), Interscience Publishers Ltd., London, 1956, p. 191.
[22] B.P. 778,639.

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attached to titanium atoms and that the absorbed olefin then reacts with the complex anions in the lattice:

$$Ti^{3+}\leftarrow\!\!\!\!\!\!\begin{matrix}CH_2\\ \|\\ CH_2\end{matrix} + \bar{C}l\bar{A}lR_3 \longrightarrow \overset{+}{T}iCH_2{\cdot}CH_2R + AlR_2Cl$$

Polymerisation at each centre then proceeds by interposition and chain-transfer reactions similar to those occurring during the interaction between ethylene and aluminium alkyls discovered by Ziegler.[23] This mechanism would give the end groups, R and $C{:}CH_2$, found experimentally by Natta and his co-workers.[16]

$$\overset{+}{T}i{\cdot}CH_2{\cdot}CH_2R + nC_2H_4 \longrightarrow \overset{+}{T}i{\cdot}CH_2{\cdot}CH_2{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}R$$

$$\overset{+}{T}i{\cdot}CH_2CH_2{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}R + C_2H_4 \longrightarrow \overset{+}{T}i{\cdot}CH_2{\cdot}CH_3 + CH_2{:}CH{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}R$$

A second mechanism, which gives the same end groups, may be postulated in which bivalent titanium reduces ethylene with the liberation of a hydride ion:

$$Ti^{3+} + CH_2{:}CH_2 \longrightarrow Ti^{3+}{\cdot}CH{:}CH_2 + H^-$$

The hydride ion passes into the lattice while chain propagation proceeds by interposition, and termination by reaction of the active centre with a complex anion from the lattice.

$$Ti^{3+}{\cdot}CH{:}CH_2 + nC_2H_4 \longrightarrow Ti^{3+}{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}CH{:}CH_2$$

$$\bar{A}lR_2Cl + Ti^{3+}{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}CH{:}CH_2 \longrightarrow Ti^{3+} + R{\cdot}[CH_2{\cdot}CH_2]_n{\cdot}CH{:}CH_2 + AlR_2Cl$$

The authors thank their colleagues, particularly Drs. J. W. C. Crawford and P. A. Small, at the Research Department of this Division, for discussions, and Mr. M. E. A. Cudby for technical assistance. Infrared absorption spectra were measured by Messrs. R. G. J. Miller and H. A. Willis, and analyses performed by the Division Analytical Department.

IMPERIAL CHEMICAL INDUSTRIES LIMITED, PLASTICS DIVISION,
WELWYN GARDEN CITY, HERTS. [*Received, July 30th*, 1958.]

[23] Ziegler, *Angew. Chem.*, 1952, **64**, 323.

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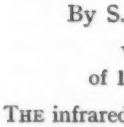
161. *Spectra of Acetals. Part I. The Infrared and Raman Spectra of* 1 : 3-*Dioxolan.*

By S. A. BARKER, E. J. BOURNE, R. M. PINKARD, and D. H. WHIFFEN.

Values have been assigned to 25 of the 27 fundamental vibrational modes of 1 : 3-dioxolan, as indicated in Table 2.

THE infrared spectra of 1 : 3-dioxolan (I), together with a number of substituted dioxolans and acyclic acetals and ketals, have been reported [1,2] over a limited range (1030—1190 cm.$^{-1}$) and some assignments suggested. The Raman and infrared spectra (see Figure) of 1 : 3-dioxolan are now reported and assigned. The aim of this research was the eventual application of this knowledge to the interpretation of the spectra of sugar acetals and ketals containing substituted dioxolan ring systems.



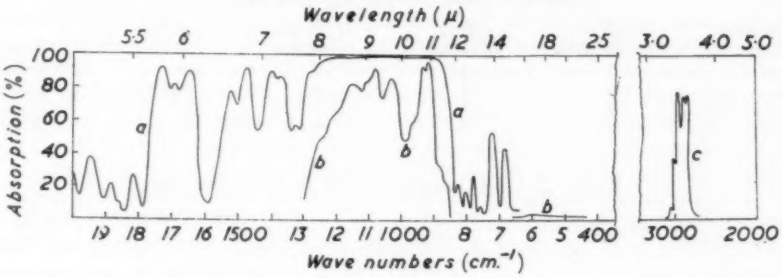
(I)

The exact geometry of the dioxolan ring is not known although Mills [3] suggested that the ring is nearly planar. However, the diffuse nature of the Raman lines and breadth of the infrared bands indicated a puckered ring. In the region 1200—1300 cm.$^{-1}$, 1 : 3-dioxolan shows a broad band in its Raman spectrum which stretches over *ca.* 70 cm.$^{-1}$ and

[1] Bergmann and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 161.
[2] Lagrange and Mastagli, *Compt. rend.*, 1955, **241**, 1947.
[3] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 13.

is just identifiable as two very broad diffuse lines. The corresponding infrared bands were so broad and ill-defined that the centres were difficult to locate. Similar broad bands were present in the spectra of *cyclo*pentane and tetrahydrofuran, which are known to be

Infrared spectrum of 1 : 3-*dioxolan, b. p.* 74—75° (*singe peak on vapour chromatography,* (*a*) *in* 0·1 *mm. cell,* (*b*) *as liquid film, and* (*c*) *in* CCl_4.



puckered,[4,5,6] but were absent from the spectrum of 1 : 3-dioxol-2-one,[7] which is known to be planar.

Experimental

Purification of 1 : 3-*Dioxolan.*—Commercial 1 : 3-dioxolan (34 ml.) and lead dioxide (3 g.) were heated under reflux for 2 hr., cooled, and filtered. Xylene (40 ml.) and lead dioxide (2 g.) were added to the filtrate and the mixture fractionally distilled. Xylene (20 ml.) and sodium wire (*ca.* 3 g.) were added to the main fraction, b. p. 70—71°, and, after the vigorous reaction had subsided, the mixture was refractionated and the main fraction, b. p. 73—74°, collected. Sodium wire was added to the product from the first fractionation, and after refractionation the fraction of b. p. 74—75° was collected.

Measurement of Spectra.—The Raman spectra were recorded photographically on a Hilger Raman spectrometer, with a filter solution[8] containing 4% of *p*-nitrotoluene and 1 part in 12,000 of Rhodamine 6GBN 500 (supplied by Imperial Chemical Industries Limited) which, because of decomposition by the mercury-lamp source, was renewed after every 4 hours' exposure. The filter solution transmitted 86% of the exciting line (4358 Å), the transmission falling off rapidly on either side of this wavelength. The transmission of the strong mercury lines at 4047 and 4078 Å was reduced to $<6\%$ and $<12\%$ respectively, and that of a barium impurity at 4554 Å to 58%.

The Raman lines were measured within ± 1 cm.$^{-1}$ against standard iron-arc lines. Qualitative polarisation data were obtained from exposures with polaroid wrapped around the Raman tube.[9]

The infrared spectra were measured on a Grubb-Parsons single-beam spectrometer with a sodium chloride and a potassium bromide prism. The carbon–hydrogen stretching frequencies were measured in the third order on a grating spectrometer having a 2500 lines/inch grating. Measurements were carried out in the vapour state, in liquid films of 0·02—0·1 mm. thickness, and as solutions (M/3) in carbon tetrachloride.

Discussion

Since the degree of puckering in the dioxolan ring is probably small[4] the symmetry will not deviate far from that of a planar ring. Application of the selection rules[10] to

[4] Kilpatrick, Pitzer, and Spitzer, *J. Amer. Chem. Soc.*, 1947, **69**, 2483.
[5] Miller and Inskeep, *J. Chem. Phys.*, 1950, **18**, 1519.
[6] Le Fèvre and Le Fèvre, *Chem. and Ind.*, 1956, 54.
[7] Angell, *Trans. Faraday Soc.*, 1956, **52**, 1178.
[8] Edsall and Wilson, *J. Chem. Phys.*, 1938, **6**, 124.
[9] Crawford and Horwitz, *ibid.*, 1947, **15**, 268.
[10] Herzberg, " Infra-red and Raman Spectra of Polyatomic Molecules," Van Nostrand, New York, 1945.

such a planar ring (cf. ref. 5) indicates that twenty-seven normal vibrations are expected for 1 : 3-dioxolan and these are shown, according to the symmetry class to which they belong, in Table 1. The molecule has a two-fold axis (the z axis) and two planes of symmetry, that of the ring (yz) and that through the two-fold axis and perpendicular

TABLE 1. *Selection rules for* 1 : 3-*dioxolan.*

Symmetry class	Total no. of vibrations	Ring vibrations	Hydrogen vibrations	Infra-red	Raman
A_1	9	4	5	*Mz*	Polarised
A_2	5	1	4	Inactive	Depolarised
B_1	6	1	5	*Mx*	Depolarised
B_2	7	3	4	*My*	Depolarised

TABLE 2. *Assignments (cm.$^{-1}$) for* 1 : 3-*dioxolan.*

Activity	Vibration	Assignment (cm.$^{-1}$) Infrared	Raman
	Symmetry class A_1		
Infrared parallel z, B band, Raman polarised	Sym. C–H stretch (C_2)	2857s	2852m d PP
	Sym. C–H stretch (C_4, C_5)	2889s	2894vs b P
	CH_2 scissors (C_2)	1509s	1509s shp
	Sym. CH_2 scissors (C_4, C_5)	1480s	1481s shp
	Sym. CH_2 wag (C_4, C_5)	1361s sh	1352w
	Ring stretch	1087vs	1088w m PP
	Ring stretch	1030vs	1038vw
	Ring stretch (breathing)	939vs	939vs shp P
	Ring bend (in-plane)	NI	658vw
	Symmetry class A_2		
Infrared inactive, Raman depolarised	Antisym. C–H stretch (C_4, C_5)	—	2972s bd
	CH_2 twist (C_2)	(1251)w vb	1246m vb
	Antisym. CH_2 twist (C_4, C_5)	(1208)w vb	1210m vb
	Antisym. CH_2 rock (C_4, C_5)	—	1009w
	Ring bend (out-of-plane)	—	—
	Symmetry class B_1		
Infrared, parallel x, C band, Raman depolarised	Antisym. C–H stretch (C_2)	2998m	—
	Antisym. C–H stretch (C_4, C_5)	2964s	(2972)s bd
	Sym. CH_2 twist (C_4, C_5)	1286w sh	—
	CH_2 rock (C_2)	723m	725w—m
	Sym. CH_2 rock (C_4, C_5)	921vs	—
	Ring bend (out-of-plane)	—	—
	Symmetry class B_2		
Infrared, parallel y, A band, Raman depolarised	Sym. C–H stretch (C_4, C_5)	2889s	2894vs bd
	Antisym. CH_2 scissors (C_4, C_5)	1480s	1481s shp
	CH_2 wag (C_2)	1397s	1397w—m
	Antisym. CH_2 wag (C_4, C_5)	1327w	1329w
	Ring stretch	1158vs	—
	Ring stretch	961s sh	962w—m
	Ring bend (in-plane)	680m	671vw

Key: v, very; s, strong; m, medium; w, weak; P, polarised; PP, partially polarised; b, broad; d, diffuse; sh, shoulder; shp, sharp; NI, not investigated.

to the plane of the ring (xz). (These axes are chosen in accordance with the latest recommendations.[11]) Dioxolan therefore belongs to the point group C_{2v}. The assignments made are in Table 2. (Evidence for certain of the assignments was obtained from the spectra of substituted dioxolans which are given in the following paper.)

Symmetrical C–H *Stretching Vibrations.*—By analogy with the *cyclo*pentane spectrum these vibrations would be expected near 2870 cm.$^{-1}$. The absorption (2857 cm.$^{-1}$) assigned to the symmetrical C–H stretching vibration of the 2-methylene group is also shown by 4-methyldioxolan, but not by any of the 2-substituted dioxolans. The corresponding

[11] Report on Notation for the Spectra of Polyatomic Molecules, *J. Chem. Phys.*, 1955, **23**, 1997.

Raman line (2852 cm.$^{-1}$) was too diffuse to determine whether, as would be predicted, it was polarised. The two symmetrical C–H stretching vibrations of the 4- and the 5-methylene group were allocated to almost the same frequency (infrared 2889 cm.$^{-1}$; Raman 2894 cm.$^{-1}$) as that assigned by Angell [7] to similar vibrations in dioxol-2-one.

Antisymmetrical C–H *Stretching Vibrations.*—Although a Raman line corresponding to the infrared band (2998 cm.$^{-1}$) assigned to the antisymmetrical C–H stretching vibration (B_1) of the 2-methylene group has not been observed, the Raman line at *ca.* 2972 cm.$^{-1}$ is very broad and diffuse and stretches up to *ca.* 2990 cm.$^{-1}$. A comparison with the substituted dioxolans is not possible for this frequency, as in these compounds it is overlaid by a methyl vibration. To the out-of-phase antisymmetrical C–H stretching vibration (A_2) of the 4- and the 5-methylene group has been assigned the strong diffuse Raman line at 2972 cm.$^{-1}$, and the strong infrared band at 2964 cm.$^{-1}$ has been assigned to the corresponding in-phase vibration (B_1). The two frequencies are close and the Raman line corresponding to 2964 cm.$^{-1}$ is probably overlaid by the diffuse line at 2972 cm.$^{-1}$. The assignment of the higher frequency to the out-of-phase vibration is in agreement with Angell's [7] assignments for dioxol-2-one, although in this case there is a difference in frequency of some 40 cm.$^{-1}$.

Methylene Scissoring Vibrations.—The frequency (1509 cm.$^{-1}$) assigned to the scissoring vibration of the 2-methylene group is also displayed by 4-methyldioxolan but not by any 2-substituted dioxolan. The corresponding in-phase (A_1) and out-of-phase (B_2) scissoring vibrations of the 4- and the 5-methylene group have been assigned the same frequency (1480 cm.$^{-1}$): this coincidence is supported by the decrease in intensity, without alteration in frequency, when one of these groups is substituted. The Raman line at 1480 cm.$^{-1}$ appears depolarised, but this is not unexpected as the polarised A_1 line is overlaid by the depolarised B_2 line. It is of interest that the frequency increases as the methylene group is linked first to one oxygen atom (–O–CH_2–C–) and then to two (–O–CH_2–O–) (cf. methylene scissoring vibrations in *cyclo*pentane, 1455 cm.$^{-1}$; in tetrahydrofuran, 1450 and 1489 cm.$^{-1}$).

Methylene Wagging Vibrations.—Here again comparison of previous assignments of methylene wagging modes in *cyclo*pentane,[5] tetrahydrofuran,[12] and dioxol-2-one [7] indicate that attachment of a methylene group to an oxygen atom increases its frequency. Hence the wagging vibration frequency of the 2-methylene group has been assigned the value 1397 cm.$^{-1}$, and the symmetrical (A_1) and antisymmetrical (B_2) wagging vibrations of the 4- and the 5-methylene group the frequencies 1361 and 1327 cm.$^{-1}$, respectively. All three assignments are supported by the spectra of the substituted dioxolans.

Methylene Twisting Vibrations.—The appearance of a weak infrared band at *ca.* 1251 cm.$^{-1}$ is probably due to the fact that selection rules do not apply strictly in the liquid state since the moderately strong Raman line at *ca.* 1246 cm.$^{-1}$ assigned to the twisting vibration (A_2) of the 2-methylene group is also shown by 4-methyldioxolan but not by 2-methyl- or the 2 : 4-dimethyl-dioxolans. The other A_2 twisting vibration, the antisymmetrical one involving the 4- and the 5-methylene group, has been assigned to the moderately strong Raman line at *ca.* 1210 cm.$^{-1}$. The assignment of the weak infrared band at 1286 cm.$^{-1}$ to the corresponding symmetrical vibration (B_1) is less certain because no information was available on the direction of the change of dipole moment. For both the twisting vibrations and the rocking vibrations discussed below, the oxygen atom does not appear to have a recognisable effect on frequencies.

Methylene Rocking Vibrations.—The frequency (723 cm.$^{-1}$) assigned to the rocking vibration of the 2-methylene group is also displayed by 4-methyldioxolan but not by the 2-substituted dioxolans. The weak Raman line at 1009 cm.$^{-1}$ has been assigned to the antisymmetrical rocking vibrations of the 4- and the 5-methylene group, since there is no corresponding infrared band as required by the symmetry type (A_2). The analogous symmetrical vibration (B_1) has been assigned the frequency of the strong infrared band

[12] Tschamler and Voetter, *Monatsh.*, 1952, **83**, 302.

at 921 cm.$^{-1}$. The corresponding Raman line has not been observed, as is consistent with a rocking vibration.

Ring Vibrations.—Four of the five ring stretching vibrations are readily identified since they give rise to intense infrared lines which are also present in the spectra of the substituted dioxolans. The frequency at 939 cm.$^{-1}$ can be unequivocally assigned to the ring breathing vibrations (A_1) since it is the strongest Raman line below 1500 cm.$^{-1}$ and is highly polarised. The higher frequency (cf.: tetrahydrofuran, 913 cm.$^{-1}$; *cyclo*pentane, 886 cm.$^{-1}$) was to be expected on introduction of a further oxygen atom into the ring. The polarisation of the Raman line corresponding to the infrared band at 1087 cm.$^{-1}$ indicates that this ring stretching vibration is of the A_1 symmetry class. Although the Raman line at 1038 cm.$^{-1}$ was too weak for the polarisation to be ascertained, the corresponding infrared absorption at 1030 cm.$^{-1}$ showed a band shape indicating [13] a dipole moment change parallel to the z axis. This frequency has therefore been assigned to an A_1 vibration. Bergmann and Pinchas [1] also assigned this band to a symmetrical ring stretching vibration.

One of the two remaining ring stretching vibrations, which should be of the B_2 symmetry type, has been assigned to the very strong infrared band at 1158 cm.$^{-1}$, in agreement with Bergmann and Pinchas [1] who assigned this to an antisymmetrical stretching vibration. The other ring stretching vibration is assigned tentatively the value 961 cm.$^{-1}$.

The A_1 in-plane ring deformation has been assigned to the weak Raman line at 658 cm.$^{-1}$. The Raman line is too weak for polarisation data but in the 2 : 2-dimethyldioxolans the intensity of the corresponding line at 638 cm.$^{-1}$ is very much enhanced by coupling of the in-plane ring deformation with the symmetrical stretching vibration of the *gem*-dimethyl group. The corresponding line in 2 : 2-dimethyl-1 : 3-dioxolan, which has the same symmetry as 1 : 3-dioxolan, is strongly polarised. The B_2 in-plane deformation has been assigned the moderately strong infrared band and weak Raman line at *ca.* 680 cm.$^{-1}$. A strong infrared band has been observed near this frequency in some, and a Raman line in all but one, of the substituted dioxolans, confirming the assignment of this frequency to a ring vibration. The two assignments (658 and 680 cm.$^{-1}$) reflect the upward trend of frequency with introduction of oxygen atoms into the ring system (cf. in-plane ring deformation of *cyclo*pentane, 545 and 617 cm.$^{-1}$; in-plane ring deformations of tetrahydrofuran, 596 and 650 cm.$^{-1}$).

The two fundamentals to which frequencies have not been assigned are the out-of-plane ring frequencies. These almost certainly lie below the limit of infrared measurements (420 cm.$^{-1}$) and have not been observed in the Raman effect. If the out-of-plane puckering can occur at different ring atoms, the interchange co-ordinate between the puckered arrangements accounts for one of the degrees of freedom for the out-of-plane deformation. This motion is not describable by a simple harmonic motion and would need to be treated by special methods, as would the second out-of-plane ring motion, which would depend largely on the atom which was instantaneously out of the plane.

The failure of the infrared spectrum of 1 : 3-dioxolan vapour to show recognisable band shape, with one exception at 1030 cm.$^{-1}$, has been a serious handicap in the assignment of frequencies. The polarisation of the Raman lines has only been a little more helpful, for of the five polarised lines expected below 1400 cm.$^{-1}$, only one highly polarised line and one partially polarised line have been observed as polarised.

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[13] Gerhard and Dennison, *Phys. Rev.*, 1933, **43**, 197; Badger and Zumwalt, *J. Chem. Phys.*, 1938, **6**, 711.

162. *Spectra of Acetals. Part II.* The Infrared and Raman Spectra of Substituted* 1 : 3-*Dioxolans.*

By S. A. Barker, E. J. Bourne, R. M. Pinkard, and D. H. Whiffen.

Assignments have been made for some of the frequencies of several substituted 1 : 3-dioxolans; a few of the vibrational modes were not identifiable. The hydroxyl group in 4-hydroxymethyl-2 : 2-dimethyldioxolan has been deuterated, enabling the frequencies associated with this group to be identified. Some assignments, based on this work, have been suggested for three hexitol ketals.

Ethylidene and *iso*propylidene acetals of ethylene and propylene glycol, which were all methyl-substituted dioxolans, were chosen for study since the effect, on the spectra, of substitution at each position in the dioxolan ring could then be observed since the methyl groups gave comparatively few and well-known characteristic frequencies. 4-Hydroxymethyl-2 : 2-dimethyldioxolan, together with its *O*-deutero-analogue and its methyl ether, were studied to observe the effect of the hydroxyl group, for correlation with the spectra of the sugar acetals and ketals.

Experimental

Preparation of Substituted Dioxolans.—2-Methyl-1 : 3-dioxolan, prepared by Hibbert and Timm's method,[1] had b. p. 82°/751 mm.

4-Methyl-1 : 3-dioxolan, obtained by condensation of propylene glycol and paraformaldehyde in the presence of syrupy orthophosphoric acid,[2] had b. p. 84°/736 mm.

An exchange reaction between acetaldehyde dipentyl acetal and propylene glycol, as performed by Lucas and Guthrie,[3] was used to afford the stereoisomers of 2 : 4-dimethyl-1 : 3-dioxolan. The separation of the isomers, their physical constants, and the assignment of configurations have been described elsewhere.[4]

2 : 2-Dimethyl-1 : 3-dioxolan, prepared by the method of Dworzak and Hermann,[5] had b. p. 92°.

2 : 2 : 4-Trimethyl-1 : 3-dioxolan, obtained [6] by condensing acetone with propylene glycol, had b. p. 101°.

Azeotropic distillation was utilised in the synthesis [7] of 4-hydroxymethyl-2 : 2-dimethyl-1 : 3-dioxolan, b. p. 85°/11 mm., n_D^{20} 1·4347. Reaction with methyl iodide and dry silver oxide [8] yielded 4-methoxymethyl-2 : 2-dimethyl-1 : 3-dioxolan, b. p. 50—51°/19 mm.

To 4-hydroxymethyl-2 : 2-dimethyldioxolan (13·2 g.) dissolved in ether (50 ml.), sodium wire (3 g.) was added. Then the excess of sodium was removed and the ether evaporated. The solid sodium salt was dissolved in deuterium oxide (2 g.), and the solution neutralised with dry carbon dioxide. 4-Deuteroxymethyl-2 : 2-dimethyl-1 : 3-dioxolan was obtained by distillation at 10^{-5} mm.

The spectra of these dioxolans, some of which were racemic mixtures, were measured as described in the preceding paper, and are recorded in the Tables.

Discussion

The assignments for the substituted dioxolans (Table 1) have been made by analogy with the assignments for dioxolan given in Part I. In assigning the internal vibrations of the methyl groups, use was made of the review by Sheppard and Simpson [9] on the spectra

* Part I, preceding paper.

[1] Hibbert and Timm, *J. Amer. Chem. Soc.*, 1924, **46**, 1283.
[2] Clarke, *J.*, 1912, 1788.
[3] Lucas and Guthrie, *J. Amer. Chem. Soc.*, 1950, **72**, 5490.
[4] Barker, Bourne, Pinkard, Stacey, and Whiffen, *J.*, 1958,
[5] Dworzak and Herrmann, *Monatsh.*, 1930, **52**, 83.
[6] Boeseken and Hermans, *Rec. Trav. chim.*, 1923, **42**, 1104.
[7] Newmann and Renoll, *J. Amer. Chem. Soc.*, 1945, **67**, 162
[8] Baer and Fischer, *J. Biol. Chem.*, 1939, **128**, 463.
[9] Sheppard and Simpson, *Quart. Rev.*, 1953, **7**, 19.

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TABLE 1. *Assignments (cm.$^{-1}$) for the substituted dioxolans.*

Assignment	2-Me	4-Me	*cis*-2 : 4-Me$_2$	*trans*-2 : 4-Me$_2$	2 : 2-Me$_2$	2 : 2 : 4-Me$_3$	4-HO·CH$_2$-2 : 2-Me$_2$	4-MeO·CH$_2$-2 : 2-Me$_2$	4-DO·CH$_2$-2 : 2-Me$_2$	
1st overtone of CH_2 scissors (C_2) 2 × 1506 cm.$^{-1}$		3019vw								IR
		3019w								R
1st overtone of Me antisym. band (2 × 1460 cm.$^{-1}$) perturbed by resonance with Me sym. C–H stretch	2946w	2939m	2940m	2939m	2943w	2939s	2933m 2945m	2939s		IR
	2940vs P	2934s P	2934vs P	2934vs P	2936vs P	2936vs P	2938vs P	2937vs P		R
CH_3 (C_2) antisym. C–H Me (C_2) stretch	2997s	2982s *	2994s	2994s	2995vs	2995vs	2995vs	2995vs		IR
	2997vs b	2983vs b *	2982vs b *	2984vs b *	2991vs	2986vs b *	2991vs *	2991vs *		R
Me antisym. C–H stretch (C_4)		2982s *	2985s	2981s		2981s sh	2986sh	2987sh		IR
		1983sb *	2982vs b *	2984vs b *		2986vs b *	2991vs *	2991vs *		R
CH_3 antisym. C–H stretch (C_4, C_5)	2961w				2963w					IR
	—				—					R
Lone C–H stretch (C_4)		2898w	2902w sh	2902w sh		2898w	2899w sh	2899s		IR
		—	—	—		—	—	—		R
CH_3 (C_4, C_5) sym. C–H Me (C_2, C_4) stretch	2886s	2879s	2884s	2879s	2885vs	2878s	2888s	2886vs		IR
	2885s b P	2876s b P	2874vs b P	2872vs b P	2875vs b P	2868s P	*ca.* 2890vs vb P	2886vs vb P		R
CH_3 sym. C–H stretch (C_2)		2856s								IR
		?								R
OMe C–H stretch?								2820m		IR
								2815m P		R
								2841m		IR
								2835m P		R
CH_3 scissors (C_2)		1512s								IR
		1506s								R
CH_3 scissors (C_4, C_5)	1480vs	1477s	1480s sh	1477s sh	1477s sh	1479s sh	1482s sh	1480s sh	1482s	IR
	1480s	1480m	1481m	1478m	1482s	1483w	1480m	1480m		R
Me antisym. bend	1450vs	1457vs	1450vs	1448vs	1456vs	1456vs	1460vs	1458vs	1456vs	IR
	1455s	1456m	1451s	1448s	1461s	1460s	1459s	1459s		R
Me antisym. bend (*gem*-Me$_2$)					—	—	—	—		IR
					1428m	1432m	1437s	1436m		R
Lone C–H def. (C_2)	1408vs		1410vs	1408vs						IR
	—		—	—						R
Methyl sym. bend [lone C–H def (C_4)]	1381vs	1385vs	1382vs	1381vs	1374vs	1376vs	1375vs	1381vs	1377vs	IR
	—	—	—	—	1385vw	1377vw	1386vw	1380vw		R
CH_2 wag (C_2)		(1385m)								IR
		1397m								R
Sym. CH_2 wag (C_4, C_5)	1360vs				1342s *					IR
	1356w				1347w d *					R
CH_2 wag (C_5)		1336w	1339vs	1336s		1315vs	1318w	1320s	1318w	IR
		1335w	1342w	1334w—m		1314w	1331vw	1338vw		R
			1325w							

Antisym. CH_3 wag (C_4, C_5)	1309w *	1307m	1300s	1303m	1342s *					IR
?Lone C–H def. (C_2, C_4)	1320w—m	1309m	1300w	1301m	1347w d *					R
Sym. CH_3 twist (C_4, C_5)	1309w *				?					IR
	—									R
CH_3 twist (C_2)		1246w sh								IR
		1250w								R
gem-Me_2 rock					1245s	1243s	1251s	1250s	1251vs	IR
					—	1249w	1240w—m	1259w		R
gem-Me_2 rock					1218vs *	1216vs	1212vs	1212vs	1213vs	IR
					1222m *	1220m d	1210m—s	1212w—m		R
Antisym. CH_3 twist (C_4, C_5)	1217s	1214m sh	1220s	1224s	1218vs *					IR
?Me rock (C_2, C_4) ?CH_3 twist (C_5)	1219w—m	1216w—m	1218w	1225m	1220m *					R
Ring antisym. stretch	1150vs	1162vs	1162vs	1153vs	1148vs	1169vs	1158vs	1157vs	1159vs	IR
			1141vs					1141vs		
	1151w	1149w P	1164w—m	1153m	—	—	1165vw	1164vw		R
			1144w—m					1139vw		
?Me rock (C_2)	1118vs	—	1117vs	1115vs						IR
	1120w		1116w	1117w—m						R
C–O stretch (OH)							1074vs		990s *	IR
							1079w d			R
Ring sym. stretch	1087vs	1092vs	1083vs	1084vs	1061vs	1096vs	1050vs	1052vs	1052vs	IR
	—	1077w P	1085w	1083m	1064w	1095vw	1051w	1050vw		R
Ring sym. stretch	1024vs	1008vs	1022vs	1036vs	1034s	1052vs	1025sh	1032s sh	1023s sh	IR
	1026m	1008wm d	1021w—m	1035m	1040vw	1056vw	—	—		R
?Ring antisym. stretch	?	?	947vs	943s	—	977vs	987vw	973s	990s *	IR
			947w	942w	955m	979w—m	967m	972mw		R
Ring breathing	947vs	939vs	935vs	926vs	947vs	945s	971m	953m	972m	IR
								933w		
	947? vs	938m—s P	932w	923w	946? vs	947w	955m	951w		R
?*gem*-Me_2 rock					916s	920vs	927vw	919w	919m	IR
					919w	919m	917m	915w—m		R
?*gem*-Me_2 rock					893s	873s	877m	890w	879m	IR
					889vw	876w	865w P	868w P		R
?CH_3 rock (C_4, C_5)	863vs	897s	858vs	858vs						IR
	—	901w	855w	858w						R
gem-Me_2 antisym. C–C stretch					837vs	841vs	843vs	843vs	839vs *	IR
					840w	843vw	—	836vw		R
Me–Ring (C_2, C_4) C–C stretch	838m	825s	830s	822s		841? vs *	833vs	843? vs	839vs *	IR
	838vs P	830vs P	826s P	822s P						R
gem-Me_2 sym. C–C stretch					782vs	788vs	791s	790s	791s	IR
					784vs P	789vs P	792s P	791s P		R

TABLE 1. (*Continued.*)

Assignment	2-Me	4-Me	*cis*-2 : 4-Me$_2$	*trans*-2 : 4-Me$_2$	2 : 2-Me$_2$	2 : 2 : 4-Me$_3$	4-HO·CH$_2$-2 : 2-Me$_2$	4-MeO·CH$_2$-2 : 2-Me$_2$	4-DO·CH$_2$-2 : 2-Me$_2$
?CH$_2$ rock (C$_2$)		725m							IR
		726m							R
In-plane ring def.	692s	721? m	695s	693s	—	—		—	IR
	695m	—	695w—m	694w—m	675vw	692vw		692vw	R
In-plane ring def.		614m	609m		647s	644m			IR
	637vw	619vw	622w	639w	638s P	640s P	{ 648m P { 635m P	{ 646m P { 633m P	R
gem-Me$_2$ antisym. C–C def.					509vs	514vs			IR
					512vw	516w	513w	514vw	R
Me–ring (C$_2$) C–C def.	513m P		504w	517m					IR
			504m P	525w P					R
Me–ring (C$_4$) C–C def.			473w	440m					IR
		472vw	467w	445m		471vw	473w	456vw	R
gem-Me$_2$, sym. C–C def.					353vw	351vw	347w	344vw	R
Unassigned	IR 603w	IR 652w sh	IR 458w	IR 608m	IR 527w sh	IR 600s	IR 567vs	IR 735w	IR 731w
	R 738vw	835s	518w	879s sh	1105vw	765w	608w	1077vs	825vw
	784vw	R 334vw d	527w	R 283vw	R 133vw	R 145vw	~691m	1110vs	957vw
	890vw	779vw	777vw	385vw	252vw	166vw	731w	1200vs	1107m
		1111vw	793vw	609wd PP?	565vw	~248vw	908vw	1237s	2840vs
			1244vw sh	715vw PP?	735vw	286vw	1117m	2820m	
			R 245vw	764w shp PP?	1120vw	422vw	3430vs	2841m	
			294vw	880w	1173vw	600wm d	R 316w	R 291wm PP	
			374vw	1172w		732vw	381vw	327wb	
			726vw	1364vw		815vw	420vw	372vw	
			770vw			1122vw d	600w PP?	~578vw	
			881w d			1143vw	735w P	~594vw	
			1366vw shp			2916w P	1121vw	665vw	
							1291vw	735w PP?	
							3450vw	1082vw	
								1107vw d	
								1289vw	
								2835m P	

Key: IR, infrared; R, Raman; v, very; s, strong; m, medium; w, weak; d, diffuse; b, broad; sh, shoulder; shp, sharp; P, polarised; PP, partly polarised.

* Frequency used twice.

of paraffin hydrocarbons since the arrangement of methyl groups in paraffins containing an internal tertiary carbon atom is analogous to that in methyldioxolans. In paraffins containing an internal quaternary carbon atom it is analogous to that in the *gem*-dimethyldioxolans.

Vibrations involving Methylene Groups.—Assignments for these were made by strict analogy with those for dioxolan, and many have been discussed in Part I.

Vibrations involving Methyl Substituents.—(a) *Bending.* The strong infrared band and Raman line at 1450—1460 cm.$^{-1}$ shown by all methyldioxolans has been assigned to the internal antisymmetrical methyl bending vibration. 2 : 2-Dimethyldioxolans show an additional strong Raman line at *ca.* 1430 cm.$^{-1}$ (corresponding infrared band absent), presumably due to splitting of the antisymmetrical methyl bending frequency of the *gem*-dimethyl group. The very strong infrared band at *ca.* 1380 cm.$^{-1}$ in all the methyldioxolans has been attributed to the symmetrical methyl bending vibration.

(b) *Rocking.* In contrast to the internal methyl bending vibrations the rocking modes of the methyl groups often couple strongly with the skeletal vibrations. The *gem*-dimethyl rocking vibrations have been assigned to the strong infrared bands near 1250 and 1220 cm.$^{-1}$; the corresponding Raman lines are of weak or medium intensity. These frequencies are higher than those (1210 and 1190 cm.$^{-1}$) found by Sheppard and Simpson [9] for paraffins with an internal quaternary carbon atom. The frequency near 1250 cm.$^{-1}$ is only present in 2 : 2-dimethyldioxolans. A frequency near 1220 cm.$^{-1}$ is present in all the substituted dioxolans and can be assigned to a methylene twisting vibration or methyl rocking mode in the compound where there are no *gem*-dimethyl groups. Further methyl rocking vibrations may be assigned to two of the strong infrared bands at 800—1000 cm.$^{-1}$, shown by 2 : 2-dimethyldioxolans. The most probable frequencies are *ca.* 880, *ca.* 920, and *ca.* 980 cm.$^{-1}$, if the band at *ca.* 840 cm.$^{-1}$ is assigned to the antisymmetrical carbon–carbon stretching vibration of the *gem*-dimethyl group (see below).

(c) *Stretching.* The symmetrical stretching vibration of the 2 : 2-*gem*-dimethyl group has been assigned to the very strong polarised Raman line and intense infrared band at *ca.* 790 cm.$^{-1}$. This is to be compared with a strong polarised Raman line at 685—750 cm.$^{-1}$ for the corresponding vibration in the paraffins.[9] The band at 790 cm.$^{-1}$ is only present in the spectra of 2 : 2-dimethyldioxolans, in agreement with this assignment. The corresponding antisymmetrical stretching vibration of the *gem*-dimethyl group has been assigned to the very strong infrared band at *ca.* 840 cm.$^{-1}$ (absent in the other substituted dioxolans), but could alternatively be attributed to a rocking mode with one of the other bands between 800 and 1000 cm.$^{-1}$ assigned to the stretching vibration.

The stretching of the methyl–ring bond (Me–$C_{(2)}$ or Me–$C_{(4)}$) has been assigned to the very strong polarised line at *ca.* 830 cm.$^{-1}$. The corresponding vibration in the paraffins [9] occurs near 815 cm.$^{-1}$.

(d) *Deformations involving methyl groups.* As with the stretching vibrations, these deformations can be expected at higher frequencies than corresponding vibrations in the paraffins, *e.g.*, antisymmetrical deformation of the *gem.*-dimethyl group in dioxolans, weak Raman line at *ca.* 515 cm.$^{-1}$ (corresponding vibration in paraffins,[9] weak Raman line at 480—490 cm.$^{-1}$). Similarly, the symmetrical deformation of the *gem.*-dimethyl group in dioxolans has been assigned to the weak Raman line at *ca.* 350 cm.$^{-1}$, compared with 350—305 cm.$^{-1}$ in paraffins.[9]

The polarised Raman line of medium intensity near 515 cm.$^{-1}$ in 2-methyldioxolan and *cis*- and *trans*-2 : 4-dimethyldioxolan has been assigned to the C–C deformation of a 2-methyl group. This compares with a medium-intensity Raman line at 415—450 cm.$^{-1}$, assigned to the corresponding vibration in the paraffins.[9] When the methyl group is on a carbon atom (position 4) attached to one oxygen atom rather than two, the deformation vibration in the dioxolans drops to *ca.* 470 cm.$^{-1}$. This frequency is absent in 2-methyl- and 2 : 2-dimethyl-dioxolans, in agreement with this assignment.

C–H *Deformations.*—The deformation of the single hydrogen on a tertiary carbon does

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not usually give rise to strong features in either the Raman or infrared spectra of paraffin hydrocarbons, where they occur at 1330—1360 cm.$^{-1}$ and *ca.* 1380 cm.$^{-1}$. The very strong infrared band at *ca.* 1408 cm.$^{-1}$ has been assigned to one of the deformation modes of the lone C–H group in position 2 of dioxolans. The intensity of this band is considerably enhanced and the frequency increased by the adjacent oxygen atoms. This band is only present in 2-methyl- and *cis*- and *trans*-2 : 4-dimethyl-dioxolans. The other C–H deformation vibration can probably be given the frequency near 1300 cm.$^{-1}$ although this also occurs in the 4-substituted dioxolans and might alternatively be assigned to a twisting vibration. However, the lower-frequency vibration is perhaps less affected by the oxygen atoms and occurs at a similar frequency for 2- and 4-substituted dioxolans. The higher-frequency C–H deformation (position 4) has not beeen observed, presumably because it is overlaid by the symmetrical methyl bending vibration at 1380 cm.$^{-1}$.

Vibrations involving a Hydroxymethyl Substituent.—Assignments for the O–H deformation and the C–O stretching vibration of hydroxyl groups have been discussed by Stuart and Sutherland,[10] who suggested the assignment of a band at 950 cm.$^{-1}$ to the out-of-plane O–H deformation, a band at 1370 cm.$^{-1}$ to the in-plane deformation, and a band at 1110 cm.$^{-1}$ to the C–O stretching vibration coupled with other skeletal vibrations.

Comparison of the spectra of 4-hydroxymethyl- and 4-deuteroxymethyl-2 : 2-dimethyldioxolan showed that the band at 1074 cm.$^{-1}$ disappeared from the spectra of the former and was replaced by a band at 990 cm.$^{-1}$ in 4-deuteroxymethyl-2 : 2-dimethyldioxolan. The band at 1074 cm.$^{-1}$ has therefore been assigned to the C–O stretching vibration. That this frequency is somewhat lower than that observed by Stuart and Sutherland [10] may be due to hydrogen-bonding to the ring-oxygen atoms. The bands found by them at *ca.* 1370 and 950 cm.$^{-1}$ were very broad, extending over *ca.* 200 cm.$^{-1}$ and so have not been detected with the single-beam instrument used in our work.

In the infrared spectra of the pure liquids the O–H stretching vibration in 4-hydroxymethyl-2 : 2-dimethyldioxolan gives a band at 3430 cm.$^{-1}$, while the O–D stretching vibration produced a band at 2480 cm.$^{-1}$. In each compound a weak diffuse Raman line is detectable near the frequency of the infrared band. The ratio (1 : 1·38) of the O–H to the O–D stretching frequency is in good agreement with the theoretical value of 1·41 for a pure stretch.

Ring Vibrations.—The ring vibrations at 1158 and 1087 cm.$^{-1}$ occur consistently in the substituted dioxolans. Those corresponding to the 1030 cm.$^{-1}$ symmetrical ring vibration in dioxolan itself show a large variation in frequency, presumably due to coupling of this ring vibration with the vibrations of the substituent groups.

In dioxolans substituted only in the 2-position, the ring breathing vibration is readily identifiable as a strong polarised Raman line near 940 cm.$^{-1}$. In the 4-substituted dioxolans, however, the intensity of the Raman line is considerably less and so can no longer be observed as polarised. The corresponding infrared band is strong for all but 4-hydroxymethyl- and 4-methoxymethyl-2 : 2-dimethyldioxolan, for which coupling prevents its identification. The variation of intensity of this vibration precludes its use in what might have been a promising method of differentiation of five- and six-membered acetal rings since Raman spectra of 1 : 3-dioxolan and 1 : 3-dioxan showed that the ring breathing frequency of each was the only strong polarised line below 1500 cm.$^{-1}$ (1 : 3-dioxolan, 939 cm.$^{-1}$; 1 : 3-dioxan, 834 cm.$^{-1}$). Moreover, another difficulty was that 2-methyl-1 : 3-dioxolan showed a strong polarised line at 837 cm.$^{-1}$ (due to methyl–ring bond stretching) in addition to the strong polarised Raman line at 947 cm.$^{-1}$ due to its ring breathing frequency.

The remaining ring stretching vibration (dioxolan, 962 cm.$^{-1}$) appears to couple strongly, rendering its assignment difficult in the substituted dioxolans.

Assignments for the in-plane ring deformations at *ca.* 690 and *ca.* 640 cm.$^{-1}$ are similar to that for dioxolan itself.

[10] Sutherland, *Discuss. Faraday Soc.*, 1950, **9**, 261; Stuart and Sutherland, *J. Chem. Phys.*,1952, **20**, 1977; 1956, **24**, 559.

TABLE 2. *Assignments (cm.$^{-1}$) for three hexitol ketals.*

Assignment	3 : 4-*O*-*iso*Propylidene-iditol	3 : 4-*O*-*iso*Propylidene-mannitol	3 : 4-*O*-*iso*Propylidene-sorbitol
Me antisym. bend	1456s	1452s	1458s
Me sym. bend	1378s	1375s	1380s
Lone C–H def.	1336sh	1338m	1338w
gem-Me_2 rock sym.	1242s	1239s	1258m—s
gem-Me_2 rock antisym.	1214s	1218s	1207m—s
Ring antisym. stretch	1165s	1167s	1158m—s
? Skeletal stretch	1119s	1117s	1129m—s
C–O stretch (OH)	1077s	1073vs	1095m
Ring sym. stretch	1052s	?	1064sh, 1055sh
Ring sym. stretch	1029vs	1034vs	1045vs
Skeletal stretch	1002vs	1011s	1022s
? Ring stretch, *gem*-Me_2 rock	989s	981m	994m
	952m—s	934sh	955m
? *gem*-Me_2 antisym. stretch	878s	876vs	870s
gem-Me_2 rock	856s		862s
gem-Me_2 sym. stretch	814s	814w	806s
?–CH(OH)·CH_2·OH rock	716m	713m—s	721w—m

Hexitol Ketals.—The infrared spectra of the 3 : 4-*O*-*iso*propylidene ketals of L-iditol, D-mannitol, and D-sorbitol were measured over the range 650—1500 cm.$^{-1}$; the partial assignments of frequencies shown in Table 2 were made by analogy with those for the substituted dioxolans.

With respect to this and the preceding paper, the authors thank Professor M. Stacey, F.R.S., for his interest, one of them (R. M. P.) thanks the University of Birmingham for the award of the Fenwick Scholarship, and they are deeply indebted to the British Rayon Research Association for the loan of a Raman spectrometer.

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163. *Micelle Formation by Lecithin in Benzene.*

By P. H. ELWORTHY.

The osmotic pressures of solutions of lecithin in benzene have been measured at 25° and 40°. Small micelles appear even at very low concentrations, and there is a critical micelle concentration (0·73 g. l.$^{-1}$) at which aggregation of small into large micelles begins. The equilibrium between the two types of micelle is investigated by means of the law of mass action. Certain thermodynamic functions for the system are reported.

IN spite of fairly extensive studies on aqueous sols, little of the physical chemistry of lecithin in non-aqueous solutions has been investigated. It has been shown, from ebullioscopic and dialysis experiments, that in alcoholic solution monomers are present, while in benzene a form with higher molecular weight exists.[1,2] In the present work osmotic-pressure measurements show that two types of micelle are present in benzene solutions, with a sharply defined critical micelle concentration at which the smaller micelles begin to aggregate to large micelles.

EXPERIMENTAL

A modified Schultz [3] and Wagner [4] osmometer was used (Fig. 1). The cell consisted of a B24 joint (*A*) whose foot was ground perfectly flat and polished; this rested on the membrane (*B*) which was supported by filter paper (*C*) upon a brass plate (*D*). The brass plate

[1] Price and Lewis, *Biochem. J.*, 1929, **23**, 1030.
[2] Faure and Legault-Demare, *Bull. Soc. Chim. biol.*, 1950, **32**, 509.
[3] Schulz, *Z. phys. Chem.*, 1936, *A*, **176**, 317.
[4] Wagner, *Ind. Eng. Chem. Analyt.*, 1944, **16**, 520.

was perforated with $\frac{1}{16}$" diameter holes. The cell was held firmly in place upon the membrane by a collar and screwed rods (*E*) (two of the three rods are shown in the Figure). A B7 socket (*F*) was fused to the upper end of the B24 joint, and received a B7 cone fused to the end of a capillary tube (*G*) of uniform bore (0·5 mm.). A tube (*H*) was joined to the top of the B24 joint, and was filled with mercury which prevented leakage of liquids from the cell. A mirror scale for reading the osmotic height was attached to the capillary tube.

The whole osmometer rested inside a large flat-bottomed tube (5 × 55 cm.) which contained the solvent. It was held upright inside the tube by a wire attached to the top of the capillary. The assembly was placed in a thermostat regulated at 25° ± 0·05° or at 40° ± 0·05°.

Membranes.—Circular membranes, 3 cm. in diameter, were cut from non-waterproofed Cellophane No. 600. They were soaked in 25% alcohol for 2 hr. to remove impurities, then in 50% alcohol for 24 hr. to swell them to a suitable porosity for osmotic measurements in the

FIG. 1. *Section of the osmometer.*

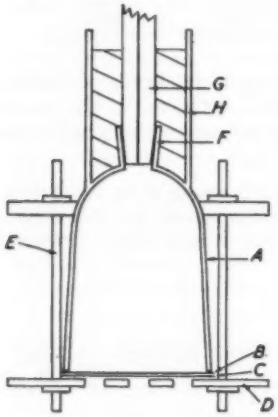
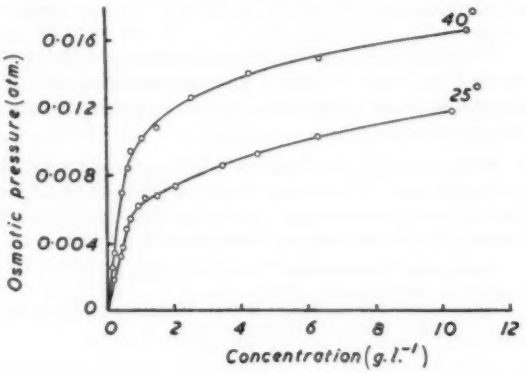


FIG. 2. *Relation of osmotic pressure to concentration at 25° and 40°.*



molecular-weight range 3000—1,000,000.[5] They were transferred through solutions of increasing alcohol content, soaked in absolute alcohol for 24 hr., and transferred to dry benzene. Tests for specific membrane effects with solvent in the cell showed no rise or fall greater than 1 mm.

Materials.—Lecithin from fresh egg yolks was prepared as previously described [6] by treatment with alumina to remove ninhydrin-reacting materials, followed by chromatography on silica gel to remove lysolecithin. After crystallisation from butan-2-one–acetone (1 : 4), the lecithin was washed with acetone and stored under dry acetone. The product (Found: N, 1·8; P, 3·8%) had $[\alpha]_D^{20}$ +7·87° (10% solution in absolute alcohol) and I no. 71.

Thiophen-free benzene, fractionally crystallised, fractionally distilled from phosphoric oxide, and stored over sodium, had b. p. 80·1°, n_D^{25} 1·4979, d_4^{25} 0·87360. Timmermans [8] gives b. p. 80·1°, n_D^{25} 1·4981, d_4^{25} 0·87368.

Method.—Solutions were prepared by thoroughly drying the lecithin in a vacuum and dissolving it in dry benzene. After assembly of the cell, during which the membrane was kept wet with solvent, the cell was washed out three times with solution, and filled so as to exclude air bubbles. It was placed in a beaker containing solvent at 25° (or 40°) and allowed to come to temperature equilibrium. This avoided, to a large extent, any thermometer effects when the assembled osmometer was placed in the thermostat.

The capillary tube was half-filled with solution, inserted into the B7 socket, and solution allowed to flow from the unseated joint until only a few cm. remained in the capillary tube;

[5] Carter and Record, *J.*, 1939, 660.
[6] Elworthy and Saunders, *J.*, 1957, 330.
[7] Elworthy, unpublished work.
[8] Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, London, 1950, pp. 145—147.

the joint was then firmly seated. The outside of the cell was washed with solvent, and mercury poured into tube (*H*). The osmometer was lowered into solvent already at the correct temperature in the large tube, and moved up and down with this tube held at an angle of 45° to remove air bubbles from below the membrane. After the osmometer had been placed perfectly upright, the large tube was stoppered.

The osmotic head was read from the mirror scale. Equilibrium was often obtained in 1 hr., and the osmometer was left overnight before final readings were taken; the osmotic head was constant for this time. After removal from the large tube, the outside of the osmometer was dried, the capillary tube and mercury were removed, and the density and concentration (by drying a portion of the solution) were determined. The capillary correction was found by using some of the solution from the cell and a piece of capillary tube identical with that of the osmometer. Very little variation of capillary rise with concentration was noted.

Results and Discussion

Fig. 2 shows the osmotic pressure at 25° and at 40° plotted against concentration. At both temperatures there is a large initial rise of osmotic pressure with concentration,

Fig. 3. *Relation of π/c to concentration at 25° and 40°.*

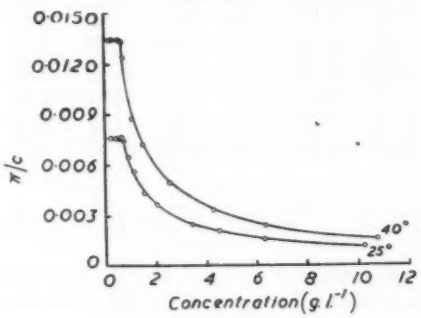
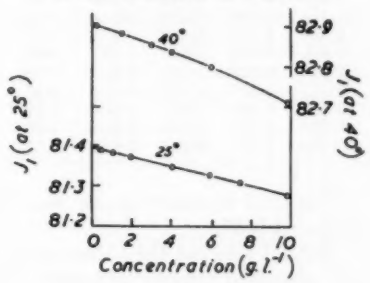


Fig. 4. *Relation of partial molar volumes to concentration at 25° and 40°.*



followed by a slower rise. Fig. 3 shows that between 0·2 and 0·73 g. l.$^{-1}$ at 25°, and between 0·2 and 0·68 g. l.$^{-1}$ at 40°, there is a constant value of π/c (where c = concentration). This indicates that, within experimental error, the molecular weight of the solute is constant in this concentration region; the average values of π/c, 0·0077 at 25° and 0·0134 at 40°, correspond to molecular weights of 3180 and 1830 respectively. Even in very dilute solutions it appears that lecithin molecules are aggregated to small micelles. Although the molecular weight at 40° was small, there was no observed decrease of the equilibrium head with time, indicating that the micelles were retained by the membrane.

The abrupt change in the properties of the curves in Figs. 2 and 3 is considered to be due to the aggregation of the small micelles into large ones, and the slow rise of osmotic pressure with concentration after the critical micelle concentration is a consequence of the formation of large micelles.

An approximate idea of the degree of aggregation of small into large micelles can be obtained by assuming that a mass-action law, without activity coefficients, applies to the aggregation:

$$\log c_2 - n \log c_1 = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where c_2 is the concentration of large micelles, c_1 is the concentration of small micelles, n is the number of small micelles aggregating into one large one, and K is a constant. The fraction x of small micelles aggregated will equal $c_2/(c_1 + c_2)$. The constants n and K are derived by successive approximation, which is illustrated for the results at 25°. At

10·299 g. l.$^{-1}$ $\pi = 0{\cdot}0118$ atm. A value of n is chosen, and also a value of x. The osmotic pressure due to the small micelles will be given by $\pi_1 = c_1RT/M_1 = 0{\cdot}0077c_1$, where M_1 is the molecular weight of the small micelles; that due to the large micelles is given by $\pi_2 = c_2RT/M_2$, where M_2 is the molecular weight of the large micelles. The total osmotic pressure, $\pi = \pi_1 + \pi_2$. M_2 is obtained from the assumed value of n, and x is adjusted till the sum of π_1 and π_2 equals the observed osmotic pressure. Values of c_1, c_2, and n are substituted into equation 1, and K is calculated. The values of n and K are used to provide the value of c_1 when $c_2 = 1$ and $\log c_2 = 0$. The total osmotic pressure at this point is calculated, and compared with the observed value. The process is repeated until the mass-action equation predicts an osmotic pressure which exactly equals the observed value at $c_2 = 1$ g. l.$^{-1}$.

TABLE 1. *Association of small into large micelles at 25° and 40°.*
(*Concns. in g. l.$^{-1}$; π in atm.*).

At 25°						*At 40°*					
c_T	c_1	c_2	x	$10^2\pi$ (calc.)	$10^2\pi$ (obs.)	c_T	c_1	c_2	x	$10^2\pi$ (calc.)	$10^2\pi$ (obs.)
0·712	0·700	0·012	0·017	0·54	0·54	0·654	0·650	0·004	0·006	0·87	0·87
0·740	0·720	0·020	0·027	0·55	0·56	0·691	0·680	0·011	0·016	0·91	0·91
0·837	0·770	0·067	0·080	0·60	0·59	0·789	0·730	0·059	0·075	0·98	0·94
0·933	0·800	0·133	0·142	0·62	0·62	0·916	0·760	0·156	0·170	1·02	0·98
1·113	0·834	0·279	0·251	0·65	0·66	1·309	0·800	0·508	0·389	1·10	1·08
1·464	0·870	0·594	0·405	0·69	0·69	1·823	0·823	1·000	0·588	1·16	1·16
1·896	0·896	1·000	0·531	0·73	0·73	2·962	0·850	2·112	0·713	1·26	1·30
2·537	0·920	1·617	0·637	0·78	0·79	4·517	0·870	3·647	0·807	1·37	1·41
3·817	0·950	2·867	0·751	0·85	0·89	6·357	0·885	5·472	0·861	1·50	1·50
6·987	0·990	5·997	0·858	1·02	1·05	8·979	0·900	8·079	0·900	1·66	1·59
8·190	1·000	7·190	0·878	1·08	1·10	10·105	0·905	9·200	0·910	1·73	1·73
10·299	1·015	9·284	0·902	1·18	1·18						

The final equation at 25° was: $\log c_2 - 17{\cdot}9 \log c_1 = 0{\cdot}8567$; at 40°, $\log c_2 - 23{\cdot}5 \log c_1 = 1{\cdot}9837$.

Table 1 sets out the values of c_T (the total concentration), c_1, c_2, x, and the observed and calculated osmotic pressures. The observed values of π agree with the calculated values fairly well over the whole concentration range studied. The mass-action treatment indicates that small concentrations of large micelles are present below the critical micelle concentration. Above it, c_2 increases rapidly for a small change in c_1, and at the highest concentrations studied most of the solute is present as large micelles.

The molecular weights of the large micelles are obtained from the values of n, the number of small micelles aggregating into one large micelle, used in the mass-action equation which fits the experimental results. At 25° $M_2 = 57{,}000$, and at 40° $M_2 = 43{,}000$. The molecular weight of the lecithin monomer can be calculated as 784, from the nitrogen and phosphorus analyses; the large micelles contain 73 monomers at 25° and 55 monomers at 40°. Both the small and the large micelles present in the solutions have, it is suggested, structure with the hydrocarbon chains directed outwards into the benzene, and the polar heads facing into the interior of the micelle. This is a reversal of the micellar structure in water. It is likely that polar materials can be rendered soluble in the interior of the micelle in benzene, while non-polar substances can be rendered soluble in water.[7]

Some Thermodynamic Functions of the Solvent in the Lecithin–Benzene System.—Density measurements on lecithin solutions were made in a stoppered pycnometer, and the results used to provide partial molar volumes, which are shown in Fig. 4. The partial molar free energies, heat contents, and entropies of the solvent were calculated from the osmotic-pressure results by using the standard thermodynamic relation. The partial molar heat content of the solvent (ΔH_1) was calculated from the temperature coefficient of osmotic pressure, and $\Delta\overline{H}_1$ was assumed to be linear over the temperature range 25—40° (see Table 2). All the thermodynamic properties conform to the same general pattern: there

is a relatively large increase for a unit change of concentration below the critical micelle concentration, and above it only a small increase. $\Delta\overline{H}_1$ and $\Delta\overline{S}_1$ reach a roughly constant value in the concentration range 2·0—10·0 g. l.$^{-1}$.

TABLE 2. *Thermodynamic functions of the solvent in the lecithin–benzene system. (Concns. in g. l.$^{-1}$; thermodynamic functions in 10^2 cal. mole^{-1}).*

Concn.	0·2	0·4	0·6	0·7	0·8	1·0	1·5	2·0	4·0	6·0	8·0	10·0
$-\Delta\overline{G}_1$ (25°)	0·30	0·61	0·91	1·05	1·14	1·25	1·37	1·47	1·75	1·99	2·16	2·30
$-\Delta\overline{G}_1$ (40°)	0·53	1·07	1·61	1·83	1·90	2·01	2·22	2·38	2·77	2·97	3·12	3·26
$\Delta\overline{H}_1$ (25°)	4·04	8·22	12·4	13·6	13·2	13·1	14·8	15·9	17·5	16·7	16·2	16·0
$\Delta\overline{S}_1$ (25°)	0·015	0·030	0·045	0·049	0·048	0·048	0·054	0·058	0·065	0·063	0·062	0·061

An ideal solution would contain monomers of lecithin, so any aggregation into micelles represents a deviation from ideality, the solvent having smaller $-\Delta\overline{G}_1$ values than ideal. The larger the degree of aggregation, *i.e.*, the larger the micelles, the smaller is the contribution which is made to $-\Delta\overline{G}_1$. The lecithin–benzene system represents an extreme

TABLE 3. *Osmotic coefficient (g) for the lecithin–benzene system at 25°.*

Concn. (g. l.$^{-1}$)	0·2	0·4	0·6	0·7	0·8	1·0	1·5	2·0	4·0	6·0	8·0	10·0
g	0·247	0·246	0·246	0·245	0·232	0·204	0·146	0·119	0·071	0·054	0·044	0·037

case of non-ideality, for even at very small concentrations there is aggregation into micelles. This is illustrated by an osmotic coefficient (*g*), the ratio of the observed osmotic pressure to the value calculated for a solution of monomers (see Table 3). *g* is small even in the region below 0·73 g. l.$^{-1}$ when small micelles are present, and decreases sharply in the region where aggregation into large micelles takes place.

I thank Dr. L. Saunders for help and advice, Mr. J. Vokes for making the apparatus, and British Cellophane Ltd. for the gift of Cellophane.

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164. *The Crystal and Molecular Structures of Tiglic and Angelic Acids. Part I. Tiglic Acid.*

By A. L. PORTE and J. MONTEATH ROBERTSON.

X-Ray analysis shows that tiglic acid crystals are triclinic, space-group C_i–$P\bar{1}$, with two molecules of $C_5H_8O_2$ per unit cell. The use of molecular Fourier transforms leads to a fairly direct determination of the structure and shows that the acid is 2-methyl-*trans*-but-2-enoic acid, confirming the accepted chemical formula. The atoms are clearly resolved on the electron-density projections and the molecule is planar except for the hydrogen atoms and the methyl group attached to the β-carbon atom, which is 0·1 Å above the mean plane. This displacement, and a small distortion of the bond angles, relieves the intramolecular overcrowding.

EXTENSIVE study has recently been made[1] of the preparation and properties of the 2-methylalk-2-enoic acids, $R{\cdot}CH_2{\cdot}CH{:}CMe{\cdot}CO_2H$. The simplest members of the series, tiglic and angelic acids (R = H), have long been known, but the geometric configurations assigned to them are based on rather indirect evidence. The present work was therefore undertaken to attempt an unambiguous determination of the position of all the atoms in space by the method of *X*-ray crystal analysis.

[1] Cason, Allinger, and Williams, *J. Org. Chem.*, 1953, **18**, 842; Cason, Allinger, and Allen, *ibid.*, 1953, **18**, 857; Cason and Ralm, *ibid.*, 1954, **19**, 1836; Ställberg-Stenhagen, *Arkiv Kemi*, 1954, **6**, 537.

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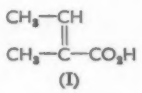
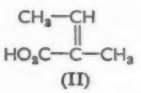
Chemical evidence indicates that tiglic acid is 2-methyl-*trans*-but-2-enoic acid (I), and angelic acid is believed to be the corresponding *cis*-acid (II). The evidence for these configurations is based on the work of Sudborough and Davies [2] on the rates of esterification



(I)



(II)

of the acids; of von Auwers and Wissebach [3] on a comparison of the physical properties of the two acids with those of the two crotonic acids of known configuration; of Pfeiffer [4] on the dibromo-derivatives of tiglic and angelic acid; and on that of Dreiding and Pratt [5] who obtained angelic acid by the carboxylation of *trans*-but-2-enyl-lithium.

The combination of all this evidence may be regarded as conclusive, but the method of *X*-ray analysis provides a more direct approach and in addition gives a complete picture of the geometry of the molecules. In particular, as these molecules may be expected to be nearly planar, the method of the molecular Fourier transform [6] may be applied to the problem. The question of configuration then reduces to that of finding which of the two possible transforms fits each reciprocal lattice.

The results described below lead to a very direct and accurate determination of the structure of tiglic acid as the *trans*-isomer. For angelic acid, described in the following paper, there are difficulties due to an abnormally high temperature factor and possible disorder. The two-dimensional methods employed, while not sufficient to yield accurate molecular dimensions, enable us to confirm the *cis*-configuration for this acid.

Crystal Data.—Tiglic acid, $C_5H_8O_2$; M, 100·1, m. p. 64·5°; d, calc. 1·164, found, 1·163. Triclinic, $a = 7{\cdot}70 \pm 0{\cdot}02$; $b = 5{\cdot}23 \pm 0{\cdot}02$; $c = 7{\cdot}42 \pm 0{\cdot}02$ Å. $\alpha = 96{\cdot}6° \pm 0{\cdot}5°$, $\beta = 86{\cdot}5° \pm 0{\cdot}5°$, $\gamma = 106° \pm 0{\cdot}5°$. No systematic absences. Space-group, C_1–$P1$ or C_i–$P\bar{1}$ (complete analysis confirms $P\bar{1}$). Two molecules per unit cell. No molecular symmetry required. Volume of unit cell = 285·6 Å^3. Absorption coefficient for *X*-rays ($\gamma = 1{\cdot}542$ Å) $\mu = 8{\cdot}56$ cm.$^{-1}$. Total number of electrons per unit cell = F(000) = 108. Thick needles developed along the b axis were obtained by slow crystallization from light petroleum. The crystals are extremely volatile and were sealed in gelatine capsules during the experiments.

Structure Analysis.—The projection of the structure along the short b axis (5·23 Å) was first studied. In the corresponding ($h0l$) zone 109 reflections were observed with Cu radiation out of a possible 151, and there appeared to be a good chance of resolving all the atoms clearly.

There are two molecules in the unit cell and it was assumed that these might exist as a centrosymmetric dimer, with hydrogen bonding between the carboxyl groups. This arrangement is very common among monocarboxylic organic acids. A simplified planar model was therefore set up, as shown at the bottom of Fig. 1, in which all the bond lengths were taken as 1·4 Å and the hydrogen bonds as 2·8 Å. On the basis of this centrosymmetric structure the Fourier transform

$$T(X^*, Y^*) = 2\sum\omega \cos 2\pi (X^*\xi + Y^*\eta)$$

was evaluated and is plotted in Fig. 1. In this expression ω is a weighting factor corresponding to the number of electrons associated with each atom.

The reciprocal net of the ($h0l$) structure factors was found to fit this transform, and the orientations of the a^* and c^* axes which give the best fit are shown in the diagram. The corresponding planar model for the *cis*-isomer leads to a transform (Fig. 1 of the following

[2] Sudborough and Davies, *J.*, 1909, **95**, 976.
[3] von Auwers and Wissebach, *Ber.*, 1923, **56**, 715.
[4] Pfeiffer, *Z. phys. Chem.*, 1904, **48**, 40.
[5] Dreiding and Pratt, *J. Amer. Chem. Soc.*, 1954, **76**, 1902.
[6] Knott, *Proc. Phys. Soc.*, 1940, **52**, 229; Klug, *Acta Cryst.*, 1950, **3**, 176.

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paper) which is similar in some respects. However, all attempts to fit the tiglic acid reciprocal net to this transform led to serious discrepancies and consequently there is no doubt that tiglic acid is in fact 2-methyl-*trans*-but-2-enoic acid.

By using the phase angles derived from the transform with the fit shown in Fig. 1 the electron density as projected on (010) was now computed by summing the appropriate double Fourier series. This gave a map in which all the carbon and oxygen atoms were clearly resolved. Structure factors calculated from the co-ordinates obtained from this map resulted in an average discrepancy (R) of 21% for the ($h0l$) zone at this stage, showing that a good approximation to the true structure had already been obtained. Application of successive difference syntheses then resulted in a final discrepancy of 11·1% for this zone, and the final electron-density map is shown in Fig. 2.

The final difference map obtained in this refinement still showed small peaks on atoms C(3) and C(4) and evidence of considerable anisotropic thermal motion, especially in the region

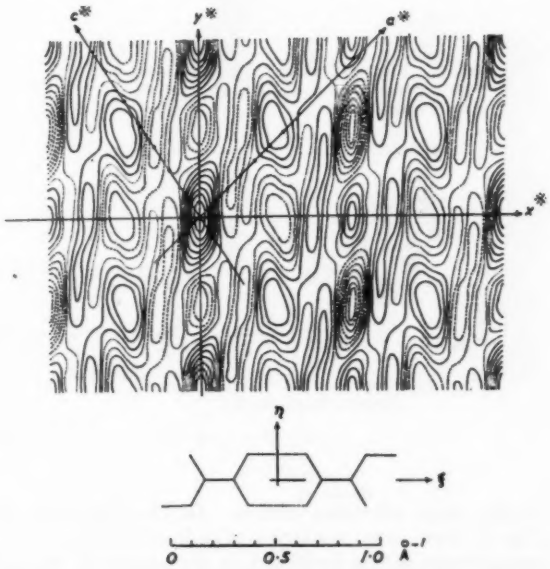


FIG. 1. *Fourier transform of idealised dimer of tiglic acid with the* a* *and* c* *reciprocal axes superimposed.*

of the oxygen atoms. No attempt was made to evaluate the anisotropic temperature factors. The mean values obtained for the Debye factors (B) for the principal projections are shown in Table 1. Those obtained from the ($0kl$) zone were not as thoroughly investigated and are less accurate. The general trend in these factors, however, indicates that the atoms furthest from the centre have the largest thermal motion, especially the terminal atoms which are bonded to only one carbon atom.

TABLE 1. *Values of* B × 10^{16} *cm.*^{2}

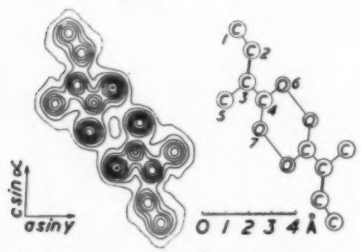
Atom	C(1)	C(2)	C(3)	C(4)	C(5)	O(6)	O(7)
($h0l$) zone	5·1	4·8	4·2	4·4	4·8	5·1	5·1
($0kl$) zone	6·2	5·1	4·0	3·8	5·8	5·1	5·1

Fig. 3 shows a difference synthesis in which the theoretical carbon and oxygen atoms each with their appropriate isotropic thermal motion have been subtracted from the observed electron distribution. The significant peaks are now due to the hydrogen atoms. There is naturally little resolution of individual atoms in this map, but although it is not possible to say exactly where a given hydrogen atom is situated, the expected number of

atoms in each neighbourhood is present. The electron density of the hydrogen atom of the carboxyl group, which is responsible for the hydrogen bonding between the molecules of the dimer, is very much smeared out, as would be expected from the electrovalent character of the bond. However, the map indicates clearly a peak of 0·6 e Å^{-2} much nearer to O(6) than to O(7). The hydrogen bond is therefore asymmetric, and the hydrogen atom concerned is bonded to O(6). It also appears to be situated slightly off the line joining the hydrogen-bonded oxygens.

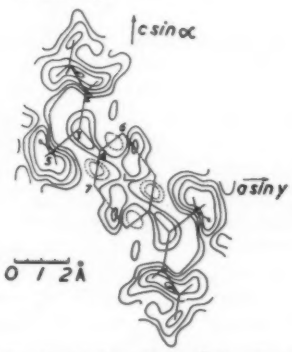
Projections of the structure along the *a* and *c* axes are shown in Figs. 4 and 5. These were prepared in the same manner as for the *b*-axis projection, but in the case of these zones the refinement process was not carried quite as far. In the (0*kl*) zone 73 reflections were observed out of a possible 97 and after refinement the discrepancy was reduced to 13·4%. Most of the atoms are very clearly resolved in this map (Fig. 4) but there is some

FIG. 2. *Electron density projection drawn on a plane normal to the* b *axis for the tiglic acid dimer.*



(Contour interval 1 e Å^{-2} with the one-electron line dotted.)

FIG. 3. *Difference synthesis for* b*-axis projection showing electron distribution due to hydrogen atoms only.*



(Contour interval 0·2 e Å^{-2}. Negative contours dotted.)

overlap with adjoining dimers. In the projection drawn perpendicular to the *c* axis (Fig. 5) there is no resolution of individual atoms, but the map demonstrates clearly the arrangement of the molecules in the unit cell. In particular it shows the origin of the very pronounced cleavage plane, $(2\bar{1}0)$, which is characteristic of these crystals. For this projection 60 structure factors were employed and the final discrepancy was 15·1%.

Co-ordinates, Molecular Dimensions, and Orientation.—The final co-ordinates are given in Table 2; *x*, *y*, *z* are expressed as fractions of the axial lengths, and *X*, *Y*, *Z* in Ångstrøm units, referred to the triclinic crystal axes. *X'*, *Y'*, *Z'*, also in Ångstrøm units, are referred to rectangular axes with *OX'* coincident with *Oa* and the plane *X'OY'* coincident with (001). The transformation relations in terms of the triclinic angles α, β, and γ are then

$$X' = X + Y\cos\gamma + Z\cos\beta$$
$$Y' = Y\sin\gamma + Z\,(\cos\alpha - \cos\beta\cos\gamma)/(\sin\gamma)$$
$$Z' = Z\,\mathrm{cosec}\,\gamma\,(1 - \cos^2\alpha - \cos^2\beta - \cos^2\gamma + 2\cos\alpha\cos\beta\cos\gamma)^{\frac{1}{2}}$$

Two independent estimates of *z* were obtained from the *a* axis and *b* axis projections (Figs. 4 and 2). The average deviation was 0·008 Å, which may be taken as an indication of the accuracy to be expected. The mean value is quoted in Table 2. The bond lengths and bond angles derived from these co-ordinates are shown in Fig. 6.

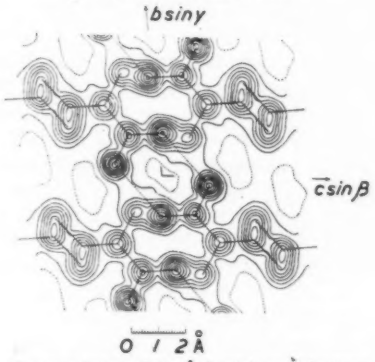
The molecule is found to be planar within the limits of probable error except for the

hydrogen atoms and the methyl group C(1) which lies 0·1 Å above the mean plane. The equation of the mean plane through atoms 2, 3, 4, 5, 6, and 7, is

$$0{\cdot}8907X' - 0{\cdot}4348Y' - 0{\cdot}1324Z' - 3{\cdot}4373 = 0$$

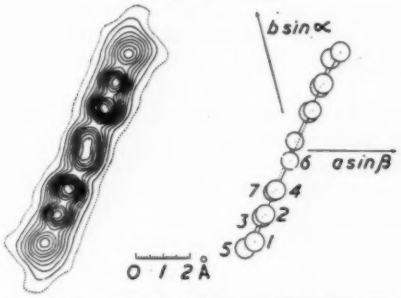
and the distances of the various atoms from this plane are given in Table 3. The orientation of the molecule in the crystal is defined by this plane and by giving the angle between the bond C(3)–C(4) and the *c* crystal axis, which is 52·8°.

FIG. 4. *Electron-density projection on a plane normal to the* a *axis.*



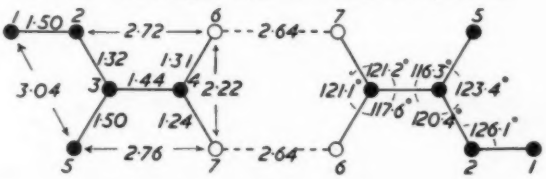
(Contour interval 1 e Å^{-2}, with one-electron line dotted.)

FIG. 5. *Electron-density projection on a plane normal to the* c *axis.*



(Contour interval 1 e Å^{-2}, with one-electron line dotted.)

FIG. 6. *Bond lengths* (Å) *and bond angles in tiglic acid.*



Accuracy.—Application of the statistical methods described by Cruickshank [7] showed the standard deviations of the atomic co-ordinates of C(1) and C(5) to be 0·012 Å; of C(2), C(3), and C(4) to be 0·009 Å, and those of the oxygen atoms to be 0·007 Å, in both the *a*- and the *b*-axis projections. From these results the standard deviation of the bond lengths

TABLE 2. *Co-ordinates.*

Atom	*x*	*y*	*z*	*X*	*Y*	*Z*	*X'*	*Y'*	*Z'*
C(1)	0·7000	0·3254	0·5557	5·3900	1·7018	4·1233	5·1725	1·2153	4·0957
C(2)	0·7863	0·5333	0·4298	6·0545	2·7892	3·1891	5·4803	2·3560	3·1677
C(3)	0·7667	0·5095	0·2523	5·9036	2·6647	1·8721	5·2834	2·3706	1·8596
C(4)	0·8707	0·7155	0·1450	6·7044	3·7421	1·0759	5·7387	3·4876	1·0687
C(5)	0·6440	0·2710	0·1506	4·9588	1·4173	1·1175	4·6364	1·2485	1·1100
O(6)	0·9773	0·9290	0·2310	7·5252	4·8587	1·7140	6·2907	4·4959	1·7025
O(7)	0·8530	0·6980	−0·0217	6·5681	3·6505	−0·1610	5·5522	3·5256	−0·1599

TABLE 3. *Distances of atoms from mean molecular plane.*

Atom	C(1)	C(2)	C(3)	C(4)	C(5)	O(6)	O(7)
d (Å).....	+0·098	0	−0·008	+0·016	+0·003	−0·014	−0·004

and those of the oxygen atoms to be 0·007 Å, in both the *a*- and the *b*-axis projections. From these results the standard deviation of the bond lengths

[7] Cruickshank, *Acta Cryst.*, 1949, **2**, 65; 1954, **7**, 519.

is found to vary from 0·012 Å for the carbon–oxygen bonds to 0·015 Å for the bond C(1)–C(2). The standard deviation of the bond angles is about 0·8°. The standard deviation of the projected electron density is 0·14 e Å^{-2} for the *b*-axis projection and 0·3 e Å^{-2} for the *a*-axis projection.

Non-bonded Distances and Molecular Arrangement.—The arrangement of the molecules in the crystal and the intermolecular approach distances are shown in Figs. 7 and 8. The closest approach occurs between the oxygen atoms of the carboxyl groups where the hydrogen bond distance is 2·64 Å, a value which is normal for this type of structure.

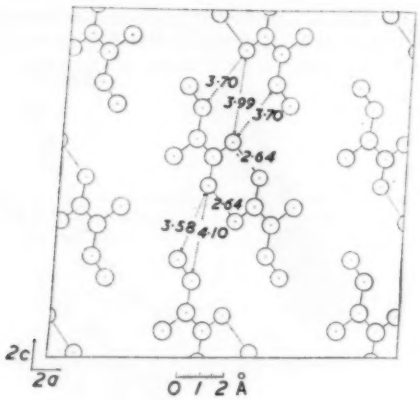


FIG. 7. *Arrangement of the molecules on the* (010) *plane.*

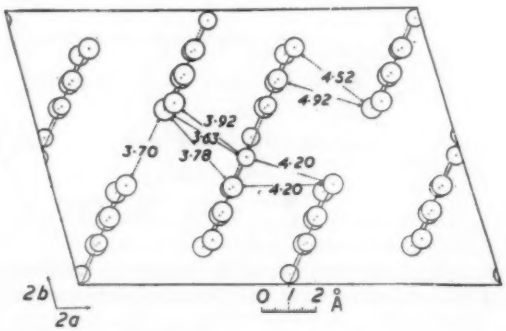


FIG. 8. *Arrangement of the molecules on the* (001) *plane.*

Between the carbon atoms the minimum approach distance, 3·70 Å, occurs in the cleavage plane between methyl groups related by a centre of symmetry, although somewhat shorter distances occur between some of the carbon and oxygen atoms. These van der Waals distances are in general of the expected order. The methyl group approach is shorter than the corresponding distances in durene and in hexamethylbenzene, but similar to those found in 2 : 3 : 5 : 6-tetramethylpyrazine and in DL-alanine. As Levy and Corey[8] have stated, when the longer non-bonded methyl–methyl distances are involved it is probable that the rotations of the methyl groups are independent of each other. With shorter distances, as in the present example, the rotations, if any, will tend to synchronise until eventually the carbon–hydrogen bonds act as cogs in rotating wheels.

Whether or not this idea applies to methyl groups in neighbouring molecules, it must be true for methyl groups belonging to the same tiglic acid molecule, if these are rotating.

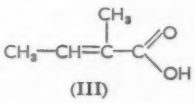
[8] Levy and Corey, *J. Amer. Chem. Soc.*, 1941, **63**, 2095.

The intramolecular distance in this case is only 3·04 Å (Fig. 6) and so it follows immediately that the hydrogen atoms of these methyl groups must have a staggered configuration. Independent rotation would mean a hydrogen atom approach of about 1·8 Å or less, which is far below what is required by the van der Waals radii.

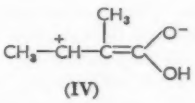
Discussion.—From Table 3 it is clear that the molecule is planar to within the limits of error except for the methyl group, C(1), which lies 0·1 Å above the plane. This is a significant departure from the plane, being about eight times the estimated standard deviation. A strictly coplanar model with bond angles of 120° would bring the methyl groups C(1) and C(5) to within 2·8 Å of one another. The distortion which allows this distance to be increased to the observed value of 3·04 Å involves an increase of the angle C(1)C(2)C(3) to 126° and a smaller increase of the angle C(2)C(3)C(5) to 123°. The overcrowding is also relieved by a rotation about the double bond C(2)=C(3) of about 4° which raises C(1) above the molecular plane by 0·1 Å. These distortions involve C(1) rather than C(5) because the latter atom is already very close to O(7), the intramolecular distance here being only 2·76 Å.

Another feature of the stereochemistry concerns the structure of the dimer. The mean molecular plane does not pass exactly through the centre of symmetry of the dimer, but is found to be at a distance of 0·05 Å from this symmetry centre. Thus the planes of the two halves of the dimer are displaced from each other by 0·1 Å. Thus indicates some departure of the O–H bond from the molecular plane, but although this hydrogen atom can be seen in the difference synthesis map (Fig. 2) it is not possible to determine its position with certainty.

The formal double bonds C(2)=C(3) and C(4)=O(7) are conjugated, and one would therefore expect some shortening of the intermediate bond C(3)–C(4). The observed shortening from a pure single sp^2 bond length of 1·50 Å is 0·06 Å and this is significant, being about five times the estimated standard deviation. According to the well-established curve correlating bond orders and bond lengths [9] the formal single bond C(3)–C(4) should therefore have a mobile bond order of about 0·5. Hence both the



(III)



(IV)

structures (III) and (IV) as well as those involving resonance within the carboxyl group must make appreciable contributions to the normal state of the tiglic acid molecule. A consequence of the polar structure is that nucleophilic reagents should attack the molecule at the β-position of the butenoic acid chain, and such reactions are known.[10]

In butadiene, $CH_2{:}CH{\cdot}CH{:}CH_2$, the formal single bond has been assigned a mobile bond order of 0·447.[11] Because of the enhanced electronegativity of oxygen it would be expected that the corresponding bond in $>C=\overset{1}{C}-\overset{1}{C}=O$ structures should have a slightly greater mobile bond order. This appears to be borne out by our results, but the accuracy is not sufficient to be conclusive.

Experimental

Cu-K_α radiation, $\lambda = 1{\cdot}542$ Å, was used in all the *X*-ray measurements. The reflections were recorded on rotation, oscillation, and moving-film photographs, and the intensities were estimated visually, use being made of the multiple-film technique and calibration wedges. Cell dimensions and triclinic angles were determined from rotation and equatorial layer-line

[9] Goodwin and Vand, *J.*, 1955, 1687.
[10] Buckles, Mock, and Locatell, *Chem. Rev.*, 1955, **55**, 659.

moving-film photographs, the angles by triangulation from diagonal translation measurements and also by measurement of the reciprocal angles from the equatorial photographs. In a preliminary account of this structure [12] less accurate values for the angles were given, and the angle γ was incorrectly given as the supplement of the angle now used (106°).

TABLE 4. *Observed and calculated structure factors.*

Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c
000	—	108·0	021	11·1	−11·7	05$\bar{1}$	3·8	−3·0	20$\bar{7}$	1·8	−1·8	50$\bar{5}$	3·1	−3·5	23$\bar{0}$	1·1	−4·7
001	6·3	7·3	022	7·6	−6·6	05$\bar{3}$	2·0	1·6	20$\bar{8}$	1·2	1·0	50$\bar{6}$	2·8	−2·0	24$\bar{0}$	1·4	2·2
002	1·1	0·5	023	5·4	−5·2	05$\bar{4}$	0·8	−0·8	301	4·1	−4·5	601	6·5	7·1	25$\bar{0}$	3·0	2·9
003	10·3	−11·8	024	8·5	7·9	05$\bar{5}$	1·8	−1·9	302	5·9	−5·7	604	2·1	−1·9	26$\bar{0}$	2·4	−3·0
004	9·0	9·4	025	1·2	1·4	061	0·8	−1·0	303	7·4	−7·2	605	5·2	4·5	310	5·8	4·4
005	6·5	6·4	026	3·4	−2·8	062	1·1	0·7	304	2·9	−3·5	606	1·5	0·9	320	2·0	2·3
006	1·6	−1·2	027	2·6	−2·0	06$\bar{1}$	0·7	−0·3	305	5·2	−4·7	60$\bar{1}$	1·8	−1·1	330	1·8	1·6
007	4·2	4·0	02$\bar{1}$	16·1	−16·8	063	1·2	1·2	306	3·4	−2·7	60$\bar{2}$	3·7	2·8	340	4·4	−3·5
008	1·2	1·5	02$\bar{2}$	16·4	−19·8	101	35·5	34·6	307	1·7	−0·5	604	1·0	1·8	31$\bar{0}$	22·5	21·3
009	1·2	0·8	02$\bar{3}$	7·8	8·6	102	4·5	4·6	30$\bar{1}$	7·6	−9·4	60$\bar{5}$	1·9	−2·2	32$\bar{0}$	3·0	0·8
010	16·8	−18·0	024	1·9	1·8	103	3·4	−3·9	30$\bar{2}$	14·4	−15·5	706	1·3	1·6	410	5·2	6·5
020	5·6	−7·2	026	10·7	−10·5	104	2·3	2·2	30$\bar{3}$	8·9	−8·9	70$\bar{1}$	2·5	1·8	420	5·3	4·4
030	5·9	5·8	027	2·4	−1·9	105	1·3	0·9	30$\bar{4}$	2·2	2·1	70$\bar{2}$	1·0	1·4	430	4·3	−4·6
040	5·9	5·5	031	10·9	11·4	106	3·3	−3·3	30$\bar{5}$	3·0	2·5	802	0·9	−1·0	4$\bar{1}$0	6·6	−6·0
050	5·9	−5·9	032	4·6	5·1	107	3·4	−3·3	30$\bar{7}$	1·7	−2·0	803	2·6	−1·6	42$\bar{0}$	20·5	25·7
100	21·0	21·9	033	2·7	−1·9	108	1·6	1·9	401	13·3	−12·5	805	1·0	−0·8	43$\bar{0}$	3·2	−2·7
200	17·3	−16·9	034	2·1	−1·6	109	1·1	1·1	402	2·9	−2·9	80$\bar{1}$	2·7	2·6	46$\bar{0}$	1·4	1·5
300	0·6	0·7	035	4·2	3·5	10$\bar{1}$	12·9	−11·8	403	3·9	−5·1	80$\bar{2}$	1·7	−1·6	510	2·4	2·2
500	3·9	2·7	036	3·8	3·4	10$\bar{2}$	16·5	−16·4	404	10·7	8·5	903	0·4	−0·7	520	2·6	1·8
600	2·5	3·4	03$\bar{1}$	1·4	−0·9	10$\bar{3}$	7·9	8·2	406	3·7	−3·1	90$\bar{1}$	1·0	−1·5	530	4·3	−3·2
800	1·6	1·7	03$\bar{2}$	5·5	5·2	10$\bar{4}$	13·5	12·9	407	2·9	−1·6	90$\bar{2}$	0·4	−1·0	5$\bar{1}$0	2·7	−0·2
011	14·0	15·8	03$\bar{3}$	1·8	2·1	10$\bar{5}$	6·1	6·5	40$\bar{1}$	9·1	−11·5	110	5·9	4·8	52$\bar{0}$	10·1	10·7
012	17·1	−20·6	03$\bar{4}$	0·8	0·6	10$\bar{6}$	1·8	1·3	40$\bar{2}$	14·4	−14·2	120	6·4	6·5	610	2·8	2·8
013	4·1	−3·2	03$\bar{5}$	2·9	−2·7	10$\bar{7}$	2·5	2·0	40$\bar{3}$	3·0	3·3	130	1·5	1·1	620	2·1	−2·4
014	7·5	−5·7	03$\bar{6}$	1·0	1·6	201	16·2	16·1	40$\bar{4}$	1·0	1·6	150	3·2	−2·4	62$\bar{0}$	2·3	−1·9
016	2·3	−1·7	03$\bar{7}$	1·2	1·1	202	20·7	−22·7	40$\bar{5}$	2·1	2·1	1$\bar{1}$0	7·7	7·1	63$\bar{0}$	5·8	7·8
017	5·2	−4·1	041	4·1	3·8	203	3·3	−3·0	40$\bar{6}$	6·3	−6·2	12$\bar{0}$	1·5	3·1	64$\bar{0}$	2·4	−1·1
018	0·6	−0·8	043	3·8	−2·6	204	7·8	−5·5	501	1·6	1·7	13$\bar{0}$	1·8	3·2	710	2·1	1·4
01$\bar{1}$	2·3	3·1	044	1·6	−1·4	206	3·0	−1·3	502	8·5	−7·7	16$\bar{0}$	1·3	−1·2	720	2·6	−2·1
01$\bar{2}$	1·7	−2·9	04$\bar{2}$	1·4	−1·7	207	5·4	−5·0	503	3·5	−3·0	210	4·9	−4·5	730	1·1	0·8
01$\bar{3}$	1·8	−1·2	04$\bar{3}$	1·6	1·0	20$\bar{1}$	5·2	6·2	504	4·5	3·6	220	7·6	8·7	7$\bar{1}$0	1·5	1·2
01$\bar{4}$	9·2	8·3	04$\bar{4}$	1·6	1·6	20$\bar{2}$	4·4	−5·3	505	6·7	6·7	230	7·1	5·3	72$\bar{0}$	1·9	−0·9
01$\bar{5}$	1·4	−1·2	04$\bar{6}$	0·6	0·6	20$\bar{3}$	1·2	−0·1	507	1·4	−1·3	240	5·8	−5·7	73$\bar{0}$	3·0	4·4
01$\bar{6}$	4·2	4·0	047	2·3	2·4	20$\bar{4}$	6·6	7·1	50$\bar{1}$	2·2	−2·2	2$\bar{1}$0	67·7	70·6	84$\bar{0}$	1·1	2·2
01$\bar{7}$	2·3	−1·8	04$\bar{8}$	2·2	1·6	20$\bar{5}$	0·9	−1·4	50$\bar{3}$	3·0	3·3	22$\bar{0}$	7·5	−7·4	94$\bar{0}$	0·6	1·6
018	2·1	1·4	054	1·1	−1·1	20$\bar{6}$	3·4	3·3									

The observed structure factors, F_o, were evaluated by the usual mosaic crystal formulæ and the calculated values F_c were obtained from the co-ordinates and the temperature-corrected scattering factors based on the calculation of McWeeny.[13]

Table 4 contains all the measured structure factors. Those too weak to be estimated have been omitted, but in these cases the calculated values were in general found to be of the expected order. The reliability index covering only the actually observed structure factors, $100\sum|(|F_o| - |F_c|)|/\sum|F_o|$, has the following values: (0*kl*) zone, 13·4%; (*h*0*l*) zone, 11·1%; (*hk*0) zone, 15·1%; overall, allowing for multiplicity of axial reflections, 13·0%.

The authors thank Professor and Mrs. E. Stenhagen for their gifts of tiglic and angelic acids, and one of them (A. L. P.) thanks the Department of Scientific and Industrial Research for the award of a research studentship during the tenure of which this work was carried out. They are also indebted to Dr. T. H. Goodwin for many helpful discussions.

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[*Received, September 29th,* 1958.]

[11] Coulson, " Valence," p. 254, Clarendon Press, Oxford, 1952.
[12] Porte and Robertson, *Nature*, 1955, **176**, 1116.
[13] McWeeny, *Acta Cryst.*, 1951, **4**, 513.

165. *The Crystal and Molecular Structures of Tiglic and Angelic Acids. Part II.*[1] *Angelic Acid.*

By A. L. Porte and J. Monteath Robertson.

Crystals of angelic acid are monoclinic, space-group C_{2h}^5–$P2_1/a$, with four molecules of $C_5H_8O_2$ per unit cell. The crystal structure was solved by use of molecular Fourier transforms, and the analysis confirms that the acid is 2-methyl-*cis*-but-2-enoic acid. Difficulties due to a high temperature factor and possible disorder restrict the accuracy with which the atomic co-ordinates can be measured. The manner in which the molecule overcomes the intramolecular overcrowding is discussed.

In the preceding paper [1] it was shown how the method of *X*-ray analysis, and especially the method of the molecular Fourier transform, may be used to assign configurations to geometrical isomers. In this way tiglic acid was shown to be 2-methyl-*trans*-but-2-enoic acid and the spatial positions of all the atoms were accurately determined. For angelic acid it has not been possible to make a very accurate structure determination. There is a high temperature factor and possible disorder. As a result only about one third of the possible *X*-ray reflections can be observed. However, the overall agreement index of 23% indicates that the structure described below is probably correct in all essential features. The molecule is found to have the *cis*-configuration. The distortions from a strictly coplanar configuration are somewhat greater than in tiglic acid but are in a direction which tends to relieve the intramolecular overcrowding.

Crystal Data.—Angelic acid, $C_5H_8O_2$; M, 100·1; m. p. 45·5°; d, calc. 1·139, found 1·141. Monoclinic, $a = 7{\cdot}66 \pm 0{\cdot}02$, $b = 11{\cdot}60 \pm 0{\cdot}02$, $c = 6{\cdot}67 \pm 0{\cdot}02$ Å, $\beta = 100 \pm 0{\cdot}5°$. Absent spectra, ($h0l$) when h is odd, ($0k0$) when k is odd. Space-group, $C_{2h}^5 - P2_1/a$. Four molecules per unit cell. No molecular symmetry is required but a centre of symmetry must lie between each pair of molecules. Volume of the unit cell = 584 Å^3. Absorption coefficient for *X*-rays ($\lambda = 1{\cdot}542$ Å) $\mu = 8{\cdot}39$ cm.$^{-1}$. Total number of electrons per unit cell = F(000) = 216.

The unit-cell dimensions agree approximately with those found by Schimper,[2] who gives $a : b : c = 0{\cdot}6494 : 1 : 1{\cdot}1393$, $\beta = 100°\ 33'$. On doubling the c axis we obtain $a : b : c = 0{\cdot}660 : 1 : 1{\cdot}150$, $\beta = 100° \pm 0{\cdot}5°$.

Crystals of angelic acid were obtained as thin plates, developed on (001), by slow recrystallisation from light petroleum. The crystals are soft and very volatile, with pronounced cleavage on (20$\bar{1}$).

Structure Analysis.—The projection of the structure along the a axis was first studied. There are four molecules of angelic acid in the unit cell and it was assumed that these formed two centrosymmetric dimers with hydrogen bonding between the carboxyl groups. A simplified planar model was therefore set up as shown at the bottom of Fig. 1. In this, it was assumed that all the bond lengths were 1·4 Å and that the hydrogen bonded O···O distance was 2·8 Å. The Fourier transform

$$T(X^*Y^*) = 2\sum\omega \cos 2\pi(X^*\xi + Y^*\eta)$$

was evaluated and is plotted in Fig. 1. Since the unit cell now contains two centrosymmetric dimers of angelic acid, the weighted ($0kl$) reciprocal lattice net cannot be obtained merely by sampling the $T(X^*Y^*)$ function but must be obtained by sampling the sum of two such transforms correctly oriented with respect to each other. By making use of the symmetry properties of the space group $P2_1/a$, it is easy to show that

[1] Part I, Porte and Robertson, preceding paper.
[2] Schimper, *Z. Kryst.*, 1881, **5**, 296.

this weighted reciprocal lattice net and the transform of one dimer are related by the expression

$$\frac{F(0kl)}{f_0} = T(0kl) + (-1)^k T(0k\bar{l}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In this, the origin of the reciprocal lattice net coincides with the origin of the transform; f_0 is the atomic scattering factor for a carbon atom, and $T(0kl)$ is the value of the transform sampled by the point $(0kl)$ of the correctly oriented reciprocal lattice.

With Cu radiation, 46 independent $(0kl)$ reflections were observed out of a possible 102. Phase angles for these were obtained by orienting the $(0kl)$ reciprocal lattice net on the $T(X^*Y^*)$ contour map until equation (1) was satisfied. Combination of these phase angles with the observed values of the corresponding structure factors, followed by summation of the appropriate Fourier series, then gave the approximate electron density as projected on to a plane perpendicular to the *a* axis of the unit cell. (For the final electron density map, see Fig. 2.) Owing to lack of resolution this map is difficult to interpret, and two

FIG. 1. *Fourier transform of idealised dimer of angelic acid with the* b* *and* c* *reciprocal axes superimposed.*

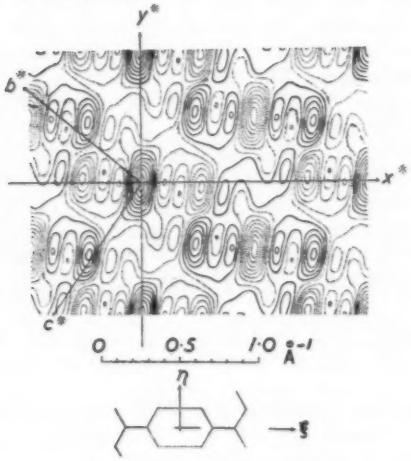
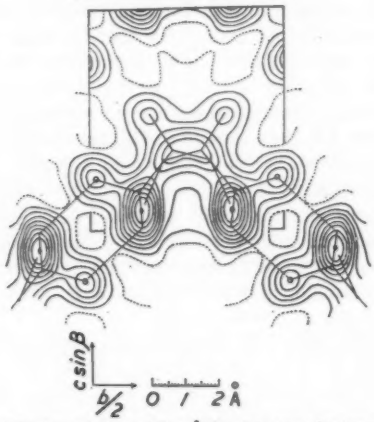


FIG. 2. *Electron-density projection on a plane normal to the* a *axis.*



(Contour interval 1 e Å^{-2}, with one-electron line dotted.)

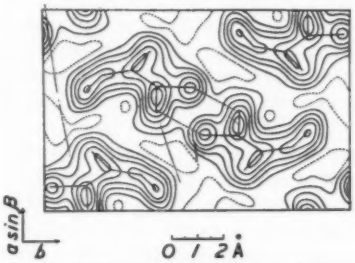
structures, each of which was approximately consistent with the postulated *cis*-butenoic acid configuration for angelic acid, could have been accepted at this stage. Furthermore, both these structures were approximately consistent with the 22 $(h0l)$ reflections which were observed and estimated, but only one of them was consistent with the observed $(hk0)$ structure factors. On the basis of this structure the *a*, *b*, and *c* axial projections were now refined independently by means of successive difference syntheses.

Structure factors calculated from the average co-ordinates obtained from the final difference maps resulted in average discrepancies (R) of 24·0% for the $(0kl)$ zone, 14·4% for the $(h0l)$ zone, and 25·4% for the $(hk0)$ zone. Although these figures are still quite high, the refinement processes were not carried further because it became impossible to interpret the difference maps unambiguously for small shifts of the atoms. In addition, the Debye factor (B) was found to be about 10×10^{-16} cm.^{2}, which made the refinement processes extremely slow. However, when the $(h1l)$ structure factors were calculated and compared with the corresponding observed values, the average discrepancy for these was found to be only 26·4%. There are no gross discrepancies between any of the observed

and calculated structure factors and all those reflections which were not observed give low calculated values. We therefore conclude that this structure is essentially correct.

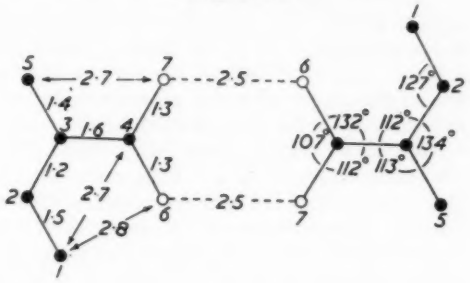
The final electron-density projections on the planes perpendicular to the *a* and *c* axes are shown in Fig. 2 and Fig. 3 respectively. These maps show conclusively that angelic acid is 2-methyl-*cis*-but-2-enoic acid.

FIG. 3. *Electron-density projection on a plane normal to the* c *axis.*



(Contour interval 1 e Å^{-3}, with one-electron line dotted.)

FIG. 4. *Approximate bond lengths* (Å) *and bond angles in angelic acid.*



Co-ordinates, Molecular Dimensions, and Orientation.—The final co-ordinates are given in Table 1; *x*, *y*, *z* are expressed as fractions of the axial lengths and *X*, *Y*, *Z* in Ångstrøm units referred to the monoclinic crystal axes; *X'*, *Y'*, *Z'*, also in Ångstrøm units, are referred to rectangular axes with *OZ'* coincident with *Oc* and *OY'* coincident with *Ob*. These are obtained from the monoclinic frame by means of the transformations

$$X' = X \sin \beta,\ Y' = Y, \text{ and } Z' = Z + X \cos \beta.$$

Two independent estimates of *x*, *y*, and *z* were obtained from the three axial projections. The averages of these are given in Table 1. The bond lengths and bond angles derived

TABLE 1. *Co-ordinates.*

Atom	*x*	*y*	*z*	*X*	*Y*	*Z*	*X'*	*Y'*	*Z'*
C(1)	0·105	0·360	0·117	0·81	4·18	0·78	0·79	4·18	0·64
C(2)	0·181	0·310	0·318	1·38	3·60	2·12	1·36	3·60	1·88
C(3)	0·207	0·213	0·361	1·58	2·47	2·41	1·56	2·47	2·14
C(4)	0·134	0·126	0·170	1·03	1·47	1·13	1·01	1·47	0·95
C(5)	0·299	0·154	0·530	2·29	1·78	3·54	2·25	1·78	3·14
O(6)	0·006	0·137	0·015	0·05	1·59	0·10	0·05	1·59	0·09
O(7)	0·124	0·017	0·231	0·95	0·20	1·54	0·94	0·20	1·38

from these co-ordinates are shown in Fig. 4. Quite large errors may be associated with these co-ordinates and we therefore do not feel justified in quoting bond lengths to more than 0·1 Å. The equation of the mean plane through the molecule, referred to the rectangular frame *X'*, *Y'*, *Z'* is $0{\cdot}8X' - 0{\cdot}6Z' - 0{\cdot}03 = 0$. This plane is very nearly the

TABLE 2. *Distances of atoms from mean molecular plane.*

Atom	C(1)	C(2)	C(3)	C(4)	C(5)	O(6)	O(7)
d (Å).....	+0·21	−0·07	−0·06	+0·18	−0·11	−0·10	−0·05

(20$\bar{1}$) plane of the crystal and accounts for the very pronounced cleavage in this plane which is characteristic of the crystals. The distances of the various atoms from this plane are given in Table 2.

Accuracy.—The resolution of the structure is poor in each of the three axial projections, and therefore Cruickshank's statistical methods [3] for estimating the standard deviations of the atomic co-ordinates cannot be applied. However, these three axial projections were refined independently of one another and therefore two independent estimates of each co-ordinate are available. The mean deviation from the mean of the two values obtained for the X and Z co-ordinates is only 0·02 Å. The deviations in the Y co-ordinates are much greater, the mean being 0·06 Å, and the largest, 0·11 Å. Probable errors of the order 0·1 Å in the bond lengths must be accepted.

Intermolecular Distances.—The closest approach occurs between the hydrogen-bonded oxygen atoms in the dimers, and was found to be 2·5 Å. The closest approach of dimers is approximately 3·3 Å and occurs between atoms C(1) of the dimer at the origin of the unit cell, and atom O(6) of the dimer centred at $\frac{1}{2}$, $\frac{1}{2}$, 0. All other non-bonded distances are of the expected order of magnitude, and the minimum values between adjacent molecules lie in the range 3·3—4·0 Å.

Discussion.—Only about one third of the reflections from the ($0kl$), ($h0l$), ($hk0$), and ($h1l$) reciprocal lattice points lying within the Cu-K_α sphere of reflection have been observed, and it is this that restricts the accuracy with which the atomic co-ordinates can be determined. The small number of observed reflections is due to the extensive overlapping of atoms in each of the projections, and especially to the high Debye factor ($B = 10 \times 10^{-16}$ cm.^{2}). Crystals of angelic acid melt at 45·5°, are extremely volatile, and appear distorted in the polarising microscope. Although no direct evidence of disorder was obtained from an examination of the X-ray photographs, it seems necessary to assume some stacking irregularities in order to account for the abnormally high temperature factor.

TABLE 3. *Observed and calculated structure factors.*

Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c	Plane	F_o	F_c
000	—	216	023	8·4	−12·9	065	2·6	−0·3	$40\bar{1}$	13·3	−11·5	250	2·2	2·6	111	5·2	5·0
001	19·0	15·7	024	5·2	7·2	072	3·6	2·3	$40\bar{2}$	25·2	29·3	280	4·0	4·5	112	15·4	−13·2
004	6·3	4·8	031	6·0	−7·9	073	4·3	2·7	$40\bar{3}$	8·5	10·6	290	5·6	−2·4	113	18·9	14·4
020	20·7	−19·1	032	21·8	−23·6	074	2·3	−0·9	$40\bar{4}$	3·5	1·8	2100	2·4	−1·4	114	5·9	9·6
040	24·1	−30·0	033	3·2	1·8	081	6·6	7·2	602	4·2	3·7	320	10·2	6·0	$11\bar{1}$	26·8	35·8
060	17·2	22·0	041	24·7	−22·2	091	3·8	−2·4	$60\bar{1}$	3·7	−1·3	330	16·9	−23·1	$11\bar{2}$	6·1	2·2
080	11·1	8·0	042	28·4	−28·3	092	4·6	−4·6	$60\bar{2}$	6·7	−3·5	340	4·6	−7·7	$11\bar{3}$	11·0	−7·9
0100	4·1	−0·8	043	3·0	3·4	0101	2·7	−1·4	110	26·8	27·5	370	4·5	3·6	$11\bar{4}$	9·1	5·3
200	9·7	−12·6	044	3·6	−0·1	0102	4·1	−2·7	120	22·1	−18·4	390	2·8	−2·4	211	10·3	−4·9
400	10·2	−7·1	051	6·3	3·6	201	16·4	−11·7	130	5·1	9·1	420	8·9	−9·2	$21\bar{1}$	32·1	−29·4
011	47·8	−54·2	052	10·0	11·5	203	3·9	4·8	150	1·8	0·4	430	9·2	−6·8	$21\bar{2}$	16·5	22·0
012	11·9	−6·5	053	3·0	4·2	204	4·5	5·5	170	7·2	6·6	440	2·0	−4·3	311	7·6	−6·2
013	8·2	−4·8	054	4·1	2·5	$20\bar{1}$	113·8	117·9	180	2·8	−1·7	450	6·5	3·9	$31\bar{2}$	8·9	15·5
014	3·8	−6·0	055	5·7	−1·3	$20\bar{2}$	24·6	24·7	210	32·6	−36·9	480	3·6	−1·6	$31\bar{1}$	14·7	15·3
015	3·9	4·1	061	3·0	2·1	$20\bar{3}$	6·3	3·9	220	17·2	19·0	490	4·4	−2·0	$31\bar{2}$	11·9	19·9
021	13·1	17·0	062	4·7	−1·1	401	4·0	5·3	230	13·8	−11·2	510	4·9	−1·5	$41\bar{1}$	9·3	−8·9
022	16·3	−15·9	063	4·3	−3·8	403	6·4	6·4	240	11·8	−13·0	520	2·7	—	$41\bar{2}$	19·6	−14·2

Although the *cis*-configuration of the acid has been confirmed, we cannot on the results of this analysis be precise about the finer details of the structure. However, it is possible to obtain a qualitative picture of the molecule from our results. In the idealised structure implied by the chemical formula, and used in the calculation of the Fourier transform shown in Fig. 1, the methyl groups lie very close to the oxygen atoms of the carboxyl group, the distance C(1)—O(6) being only 2·4 Å. The resultant steric strain might be relieved by rotating the carboxyl group out of the plane of the rest of the molecule, but this is not indicated by our results. Instead, a balance appears to be maintained between maximum overlap of π-orbitals, and hence maximum resonance, and minimum steric strain. The results show that this is achieved by a displacement of C(1), and probably also C(4), from the plane of the rest of the molecule, coupled with distortion of bond angles until the methyl groups and oxygen atoms are about 2·8 Å apart. The steric strain is not relieved by gross distortion at one particular site in the molecule but rather by smaller distortions spread over the molecule as a whole.

The intramolecular overcrowding must account in part for the differences in relative stabilities of tiglic and angelic acids and of their derivatives. If any additional strain

[3] Cruickshank, *Acta Cryst.*, 1949, **2**, 65; 1954, **7**, 519.

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should be placed on the angelic acid molecule by an attempted substitution reaction, then it may well be sufficient to cause the molecule to become completely unstable. The instability will then be overcome by rotation of the bond C(1)–C(2) about the double bond C(2)–C(3) with resultant isomerisation to tiglic acid. The ready isomerisation of angelic acid, and its derivatives, to tiglic acid, and its derivatives, has been observed.[4]

Experimental.—Cu-K_α radiation, $\lambda = 1{\cdot}542$ Å, was used in all the *X*-ray measurements. The reflections were recorded on rotation, oscillation, and moving-film photographs, and the intensities were measured visually, use being made of the multiple film technique. Unit-cell dimensions were determined from rotation and equatorial layer line moving-film photographs.

The observed structure factors, F_o, were estimated by the usual mosaic crystal formulæ and the calculated values, F_c, were obtained from the co-ordinates and the temperature-corrected scattering factors based on the calculations of McWeeny.[5]

Table 3 contains all the measured structure factors. Those too weak to be estimated have been omitted but in these cases the calculated values were in general found to be of the expected order. The overall discrepancy $100\sum|(|F_o| - |F_c|)|/\sum|F_o|$ for all the measured structure factors is 22·8%.

CHEMISTRY DEPARTMENT,
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[4] Buckles, Mock, and Locatell, *Chem. Rev.*, 1955, **55**, 659, and references therein.
[5] McWeeny, *Acta Cryst.*, 1951, **4**, 513.

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166. *Structure and Reactivity of the Oxyanions of Transition Metals. Part V.* Quadrivalent Manganese.*

By K. A. K. LOTT and M. C. R. SYMONS.

Blue solutions obtained by dissolution of manganese dioxide in hot, concentrated aqueous potassium hydroxide consist of equimolar quantities of quinquevalent and tervalent manganese.

IN an analysis of the electronic structure of certain tetrahedral oxyions,[1-3] use was made of the molecular-orbital treatment for the ions MnO_4^- and CrO_4^{2-} given by Wolfsberg and Helmholz.[3] These ions are described in terms of a " closed-shell " structure, and it was suggested that reduction of such ions involved feeding of further electrons into the first excited level, referred to by these authors as $(3t_2)$.[3] This molecular orbital is triply degenerate: however, it seems that the electron spin resonance spectrum of manganate in potassium chromate [4] is best described in terms of a level, containing the unpaired electron, which is doubly degenerate, and a preliminary study of hypomanganate in sodium vanadate appears to confirm this result. The issue is further complicated by the fact that Klemm [5] has reported a value of 3·6—3·7 B.M. for the magnetic moment of potassium hypoferrate, K_2FeO_4. If the compound studied is indeed K_2FeO_4, then this result, which is close to the free-spin value of 3·87 B.M. expected for three unpaired electrons, must mean that the orbital is at least three-fold degenerate, since if it were a doublet only one unpaired electron would be detected.

* Part IV, *J.*, 1957, 659.

[1] Carrington, Ingram, Schonland, and Symons, *J.*, 1956, 4710.
[2] Carrington, Schonland, and Symons, *ibid.*, 1957, 659.
[3] Wolfsberg and Helmholz, *J. Chem. Phys.*, 1952, **20**, 837.
[4] Carrington, Ingram, Schonland, and Symons, unpublished work.
[5] Klemm, *Angew. Chem.*, 1954, **66**, 468.

It is therefore important to obtain more information regarding this level, and accordingly one object of this research was to prepare and study oxyions having three electrons outside the " closed-shell " (for convenience we will refer to these as " outer " electrons).

A variety of syntheses have been attempted ineffectually: in this work, possible compounds containing quadrivalent manganese were studied, and although the original aim was not realised, the results bear on the general chemistry of oxyions.

Some complexes of quadrivalent manganese, *e.g.*, K_2MnCl_6,[6] are known, but little work appears to have been carried out on alkaline solutions of Mn^{IV}, though manganese dioxide dissolved in aqueous potassium hydroxide, under nitrogen, at 180° has been reported to yield manganate.[7]

Experimental and Results.

All reagents were " AnalaR," and water was doubly distilled from concentrated alkaline potassium permanganate. Hydrogen peroxide was the destabilised product supplied by Laporte Chemicals.

Preparative Procedure.—Preliminary work showed that prolonged heating of hypomanganate in concentrated potassium hydroxide solution, in Pyrex containers under nitrogen, gave intense blue-violet solutions before reduction to the characteristic red of tervalent manganese. In fused silica, solutions of hypomanganate were stable to heat, and it thus appears that impurities from the glass caused the reduction, as in the case of the reduction of Cr^{V} to Cr^{III}.[8] Reaction with oxygen re-formed hypomanganate reversibly. It was thought that the deep blue solutions observed might have contained monomeric quadrivalent manganese, and solutions for investigation were prepared by the following methods: (*a*) Known weights of pyrolusite (crude manganese dioxide) were added to potassium hydroxide–water mixtures under nitrogen, and the resulting mixture was heated by means of a luminous Bunsen flame until all the manganese dioxide had dissolved. (*b*) Known volumes of standardised potassium permanganate solution, containing potassium hydroxide, were reduced to manganese dioxide by addition of excess of hydrogen peroxide. This solution was then heated to destroy the excess of peroxide, and solid potassium hydroxide was added to the hot solution, in an atmosphere of nitrogen, until all the manganese dioxide had dissolved and the solution had become a clear blue. At room temperature the solutions set to clear glasses.

Analytical Procedure.—The net valency state of manganese in these solutions was determined by estimating the oxidising power of those containing a known amount of manganese. The melts were dissolved in an excess of potassium iodide solution, under nitrogen, and acidified, and the liberated iodine was titrated with sodium thiosulphate solution previously standardised against the potassium permanganate solutions used in experiment (*b*). A number of determinations gave a valency state of $4{\cdot}0 \pm 0{\cdot}15$.

Spectrophotometric Analysis.—Because of the difficulties encountered in measuring the absorption spectra of " glasses,"[8] a method was developed for measuring those of the fluid melts. The temperature was kept above the softening point of the melt by use of a cell-housing, for the spectrophotometer, constructed of polystyrene foam, which is an efficient heat insulator. Measurements were made on a Unicam S.P. 500 spectrophotometer, and the silica reaction tubes were employed directly as cells. To avoid errors that arise from the curvature of the surface of the tubes, a constant slit width was used. The spectrum in the wavelength region of interest was scanned without altering the position of the test solution, and in order to obtain correct values of the optical density, a procedure similar to that described previously[8] was employed.

Dissolution of pyrolusite [procedure (*a*) above] gave initially a green solution whose colour resembled that of manganate. The spectra of such solutions were not reproducible, but were qualitatively similar to that shown in Fig. 1, and do not resemble the spectrum of manganate.[9] On prolonged heating the solutions became deep blue. The spectrum (Fig. 2) is characterised by two bands centred at 480 and 670 mμ. Since it had been established that there was no overall oxidation or reduction at this stage, it was considered possible that the spectrum

[6] Weinland and Dinkelacker, *Z. anorg. Chem.*, 1908, **60**, 173.
[7] Eliot and Storer, *Proc. Amer. Acad.*, 1859, **1**, 43.
[8] Bailey and Symons, *J.*, 1957, 203.
[9] Carrington and Symons, *J.*, 1956, 3373.

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was that of a monomeric quadrivalent manganese species. However, hypomanganate has a single band in the visible region with a peak at 670 mμ,[9] and hexaco-ordinated tervalent manganese complexes generally have a single band in the 470 mμ region.[10,11] Direct measurement of the spectrum of tervalent manganese in concentrated potassium hydroxide solution confirmed this result in showing a single band in the visible region with a peak at 465 mμ, which may tentatively be ascribed to the ion $Mn(OH)_6^{3-}$. Since the apparent valency state of manganese in the blue solutions was four, it seemed probable that the constituents were hypomanganate and tervalent manganese in equimolar quantities. In order to confirm this, and to establish that none of the manganese was present in the quadrivalent state, a quantitative study of the spectra was made. From the spectra of the blue solutions after suitable adjustment for the overlapping band effect, values for the apparent extinction coefficients ($\epsilon_{max.}$) for the bands at 670 and 470 mμ were estimated to be 820 and 385 respectively. These values are based on the assumption that 50% of the manganese is present as hypomanganate (670 mμ) and 50% as tervalent manganese (470 mμ).

The extinction coefficient found for hypomanganate is very close to that of 840 estimated

FIG. 1. *Absorption spectrum of solutions of manganese dioxide in potassium hydroxide formed initially (green).*

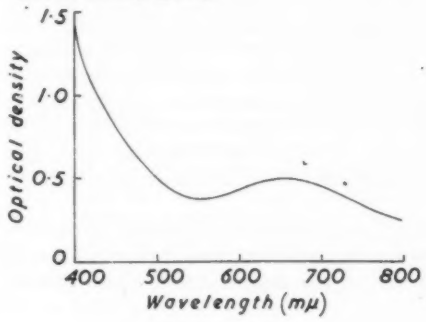
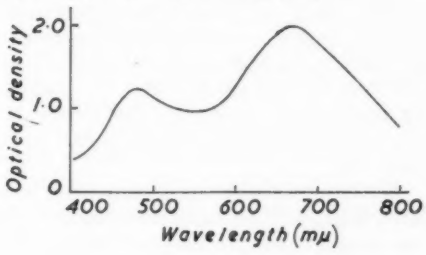


FIG. 2. *Absorption spectrum of solutions of manganese dioxide in potassium hydroxide formed after prolonged heating (blue).*



previously,[9] and was confirmed by reaction of the solutions with oxygen to convert all the manganese into hypomanganate and remeasurement of the spectrum. The results were identical with those previously recorded.[9]

It was not found possible to estimate precise values of $\epsilon_{max.}$ for Mn^{III} in concentrated alkaline solution because of the tendency of such solutions to disproportionate. However, a series of experiments in which a known quantity of bivalent manganese in aqueous potassium hydroxide was carefully oxidised with oxygen gave a value of about 340. This is undoubtedly a lower limit, but is probably correct to within 20%. The result is comparable with values of $\epsilon_{max.}$ derived from other tervalent manganese complexes in other media.

Experiments starting from potassium permanganate by procedure (*b*) gave less Mn^{V} and more Mn^{III} than required for an equimolar mixture, probably owing to partial reduction beyond the Mn^{IV} stage by hydrogen peroxide.

Magnetic Studies.—No electron spin resonance absorption, even at 20° K, was obtained from either green or blue solid solutions prepared from pyrolusite. It has been established that hypomanganate does not absorb detectably under these conditions,[1] and for similar reasons detectable resonance absorption would not be expected for Mn^{III} complexes. The six isotropic hyperfine lines characteristic of the ^{55}Mn nucleus are readily detected at room temperature from melts containing bivalent manganese. This confirms the absence of any Mn^{II} in the blue or green solutions.

Measurements of electron spin resonance spectra were made at 1·25 cm. wavelength as previously described.[1]

[10] Ibers and Davidson, *J. Amer. Chem. Soc.*, 1950, **72**, 4744.
[11] Drummond and Waters, *J.*, 1953, 435.

Discussion

Eliot and Storer's interpretation [7] that dissolution of manganese dioxide in alkali under nitrogen, at 180°, gave manganate, is in error. The green solution first formed has a variable spectrum typified in Fig. 1. We suggest that the sharp rise in the 400—500 mμ region is caused by colloidal, hydrated manganese dioxide, and that some disproportionation has already occurred. The band from Mn^{III} is presumably hidden by the absorption of the colloid. The band at 650 mμ is ascribed to MnO_4^{3-}, the apparent shift from 670 mμ being caused by the superposition of the colloid band.

There is, however, an alternative explanation. Cartledge and Ericks [12] isolated a dark green oxalato-complex of quadrivalent manganese, and recorded its spectrum in aqueous solution; this is qualitatively similar to that given in Fig. 1. The complex ion is formulated as $[Mn^{IV}(C_2O_4)_2(OH)_2]^{2-},2H_2O$ and the manganese is undoubtedly hexaco-ordinated. It therefore seemed possible that the green colour was due to a hexaco-ordinated quadrivalent manganese ion, possibly $Mn(OH)_6^{2-}$.

The electron spin resonance results are not in accord with this formulation. The ion $Mn(OH)_6^{2-}$ is isoelectronic with $Cr(OH)_6^{3-}$, both ions having three $3d$ electrons which half fill the d_ϵ level. One would expect, therefore, a temperature-independent isotropic absorption, similar to that obtained from bivalent manganese. Experimental justification for this expectation comes from the observation that tervalent chromium in a similar "glass" absorbs strongly at room temperature.[8] We therefore conclude that hexaco-ordinated quadrivalent manganese is not responsible for the green colour. It is conceivable that a tetrahedral form of quadrivalent manganese is present, but in view of the uncertainty concerning the electronic structure of tetrahedral ions of this type, mentioned above, no conclusions can be drawn from electron spin resonance results on this point.

However, the ultimate exclusive formation of hypomanganate and tervalent manganese shows that Mn^{IV} is thermodynamically unstable in this medium, and it would be very surprising if the disproportionation (3) occurred slowly at high temperatures. We therefore favour our original interpretation.

Disproportionation.—The disproportionations

$$2MnO_4^{3-} \longrightarrow MnO_4^{2-} + Mn^{IV} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and

$$2Mn^{III} \longrightarrow Mn^{IV} + Mn^{II} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

are well established and proceed to completion under ordinary conditions. Our results show, that, under conditions such that polymerisation and precipitation of quadrivalent manganese is prevented, the converse is true and the reaction

$$2Mn^{IV} \longrightarrow MnO_4^{3-} + Mn^{III} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

is virtually complete. Thus the reactions (1) and (2) are governed by the stability of polymeric manganese dioxide and by the fact that this is a solid phase. Evidently monomeric Mn^{IV} with oxide or hydroxide ligands is a very reactive species. This conclusion is in accord with an earlier discussion concerning the mechanism of reactions which result in the formation of manganese dioxide,[9] and we stress that such reactions are unlikely to proceed *via* the formation of monomeric quadrivalent manganese.

Results of kinetic studies by Merz, Stafford, and Waters,[13] involving the reduction of permanganate to Mn^{II}, suggest that Mn^{IV} species are those effective in the oxidation of

[12] Cartledge and Ericks, *J. Amer. Chem. Soc.*, 1936, **58**, 2069.
[13] Merz, Stafford, and Waters, *J.*, 1951, 638.

alcohols. Our results support the mechanism postulated by Waters *et al.* rather than the alternative by Adler and Noyes.[14] Also such steps as

$$2Mn^{VI} + Mn^{II} \longrightarrow 2Mn^{IV} \text{ (monomeric)}$$ [14]

are improbable unless certain complexing reagents are present which greatly stabilise quadrivalent manganese.

The authors thank Mr. A. Carrington, who carried out some preliminary studies, for discussion, and Dr. D. J. E. Ingram for use of the electron spin resonance apparatus. One of them (K. A. K. L.) thanks the University of Southampton for a postgraduate Research Scholarship.

THE UNIVERSITY, SOUTHAMPTON. [*Received, October 10th*, 1958.]

[14] Adler and Noyes, *J. Amer. Chem. Soc.*, 1955, **77**, 2036.

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167. *Infrared Spectra of Manganese Carbonyl Hydride and Deuteride.*

By F. A. COTTON, J. L. DOWN, and G. WILKINSON.

Infrared spectra of gaseous $HMn(CO)_5$ and $DMn(CO)_5$ in the range 3000—400 cm.$^{-1}$ are reported and discussed. The molecule appears to have very low symmetry, as Wilson also concluded, but the present interpretation of isotopic shifts differs significantly from Wilson's interpretation, notably in the assignment of the band at 1783 cm.$^{-1}$ in $HMn(CO)_5$ and the Mn–H stretching frequency.

The nuclear resonance spectrum of the hydride at 40 Mc./sec. shows a single peak at −13·0 parts per million due to a highly shielded proton such as those in other metal carbonyl hydrides.

HIEBER and WAGNER [1] have recently described the preparation of manganese pentacarbonyl hydride and some chemical and physical properties. In particular they found it to be scarcely acidic [in contrast to $HCo(CO)_4$ and $H_2Fe(CO)_4$] and their physical data suggest that the $Mn(CO)_5^-$ skeleton probably has a structure quite similar to that of iron pentacarbonyl.

The infrared spectra of gaseous manganese pentacarbonyl hydride and deuteride in the frequency range 3000—400 cm.$^{-1}$ have been studied. Although it was originally intended to examine also the region from 400 to 275 cm.$^{-1}$, the appearance of a paper by Wilson,[2] who has studied this region as well as the range which we have examined, has made this unnecessary. For the most part, Wilson's results for the hydride are in agreement with ours; however, his results for the deuteride were not given in detail and it appears from his discussions of the comparison of the spectra of the hydride and deuteride that there are errors in his data for the latter and thus also in his interpretation of the isotopic shifts.

Spectrum of Manganese Pentacarbonyl Hydride.—Present observations are listed in Table 1, together with those of Wilson for comparison. The agreement between the two sets of data is excellent. Wilson has bracketed together various groups of peaks in the 2150—1950 cm.$^{-1}$ range to indicate what he considers to be *P*, *Q*, and *R*, or *P* and *R* components of vibrational transitions. Our data are not inconsistent with such groupings but cannot be said to require them; they could conceivably be grouped in other ways. However, in any event, the complexity of the spectrum in this region makes it fairly certain that the molecular symmetry is very low, and definitely lower than C_{4v} such as the spectra [2] suggest for $XMn(CO)_5$ when X is halogen, or the pseudo C_{4v} when X is methyl. Wilson reached the same conclusions.

[1] Hieber and Wagner, *Z. Naturforsch.*, 1958, **13b**, 339.
[2] Wilson, *ibid.*, p. 349.

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It is not unreasonable to assume that the $Mn(CO)_5$ unit will adopt the same arrangement as $Fe(CO)_5$ and that the subsequent attachment of the proton will not seriously alter this geometry. Such an approach can be justified by analogy with the series $H_2Fe(CO)_4$, $HCo(CO)_4$, $Ni(CO)_4$, all of which have a tetrahedral $M(CO)_4^{n-}$ ($n = 2, 1, 0$) skeleton, and, in two of which, protons are affixed with little distortion. Two structures have been suggested for iron pentacarbonyl—the square pyramidal and the trigonal bipyramid. Although an infrared study [3] has suggested that the former is correct, Lippincott's studies [4] and other infrared and Raman spectral evidence [5] to be described shortly favour the latter model, which was originally proposed by Ewens and Lister [6] on the basis of electron-diffraction studies. If iron pentacarbonyl and hence also the $Mn(CO)_5$ unit have a square pyramidal structure, the proton might be introduced into the skeleton in several ways. It has already been concluded that it is unlikely to lie along the fourfold axis but it could, for instance, lie along a line from the manganese atom through a triangular face or through an edge of the pyramid. No such structure could have a symmetry higher than C_s and would thus have five infrared-active carbonyl stretching fundamentals.

TABLE 1. *The infrared spectra of* $HMn(CO)_5$ *and* $DMn(CO)_5$.

$HMn(CO)_5$		$DMn(CO)_5$	$HMn(CO)_5$		$DMn(CO)_5$
Wilson	Authors		Wilson	Authors	
4142 (w)			2000 }	2000 }	2000 }
4069 (w)			1994 }(vs)	1995 }(vs)	1994 }(vs)
4021 (w)			1900 }	~1900 (sh) }	~1900 (sh) }
2594 (w)	2588 (w)	2583 (w)	1978 (m)	1979 (m)	1976 (m)
2527 (w, sh)	(*a*)		1938 (m)	1940 (m, b)	1936 (m, b)
2514 (w)	2506 (w)	2509 (w)			1829 (vw)
2490 (w)	2482 (w)	2478 (w)			1801 (vw)
2459 (w) }	~2441 (w, vb)	{ 2451 (w)	1785 (m)	1783 (m)	1783 (vw)
2445 (w) }		{ 2437 (w)			1614 (w)
2400 (w)	2393 (w)	2392 (w)	1269 (w)	1271 (w)	1290 (m)
2375 (w)	(*b*)	2350 (vw)			1236 (w)
2231 (w)	2232 (w)	2230 (w)	1183 (w)	1179 (w, b)	1205 (w)
2221 (w)	2226 (w)	2224 (w)	1106 (w)	1103 (w)	1190 (w)
2199 (w)					1074 (w)
2148 (w)	2151 (w)	2150 (w)	1021 (w)	1020 (w)	1019 (w)
2128·5 }	2130 }	2130 }	989 (w)	984 (w)	989 (w)
2124·0 }(m)	2125 }(m)	2124 }(m)	915 (w)	916 (w)	891 (w)
2118·5 }	2120 }	2118 }	859 (w)	855 (w)	855 (w)
2100·5 }			760 (w)	760 (w, sh)	794 (w, sh)
2095·5 }(m)	2101 }	2103 }	730 (vs)	730 (vs)	726 (m)
2090·0 }	2097 }(m)	2096 }(m)	688 (w)	~685 (vvw)	
2064 (w)	2069 (w)	2067 (w)	669 (vs, sh)	668 (sh)	670 (vs)
2052 }(m, sh)	2051 (m)	2052 (m, sh)	663 (vs)	658 (vs)	650 (vs)
2046·5 }	2045 (m)	2047 (m)	612 (vs)	610 (vs)	606 (mw)
2033·5 }	2036 (vvs)	2034 (vvs)	558 (w)		
2028 }(vvs)	2029 (vvs)	2029 (vvs)	535 (w)	532 (vw)	536 (w)
2025·5 }	2023 }	2025 }	506 (w)	503 (vw)	511 (mw)
2020·5 }(vvs)	2016 }(vvs)	2020 (sh) }(vvs)	484 (s) (*c*)	454 (s)	452 (s)
2015 }		2015 }			

(*a*) The shoulder reported by Wilson is present in our spectrum but too poorly resolved for its frequency to be measured accurately.

(*b*) This region obscured by CO_2 absorption.

(*c*) The band listed by Wilson at 484 cm.$^{-1}$ does not appear in our spectra or in Fig. 1 of his paper. The latter does, however, show a strong peak at 21·7 μ (462 cm.$^{-1}$). We assume, therefore, that the figure 484 listed in his table is a typographical error.

For the more probable trigonal bipyramidal structure the proton might lie on lines from the manganese atom to the centre of a face, or to the centre of a slant edge (in both cases the symmetry is C_s), or on a line to the centre of an equatorial edge: the symmetry

[3] O'Dwyer, *J. Mol. Spectroscopy*, 1958, **2**, 144.

[4] Fately and Lippincott, *Spectrochim. Acta*, 1957, **10**, 8.

[5] (*a*) Stammreich, personal communication, to be published shortly; (*b*) Cotton, Danti, Fessenden, and Waugh, *J. Chem. Phys.*, in the press.

[6] Ewens and Lister, *Trans. Faraday Soc.*, 1939, **35**, 681.

would then be C_{2v}. In all these cases, however, there would be five infrared-active carbonyl stretching modes.

Hence, while we can probably rule out a C_{4v} structure, as Wilson has noted, it is impossible from analysis of C–O stretching frequencies to decide among a number of other less symmetric structures. The remainder of the spectrum provides no definite structural information since few other band assignments can be made with any certainty.

The Spectrum of Manganese Pentacarbonyl Deuteride.—Since $DMn(CO)_5$, like other carbonyl deuterides, exchanges with traces of water, care is required to obtain an authentic spectrum, and, at the same time, to interpret the results. The spectra (Table 1) indicate that the samples contained some hydride (perhaps 5—15% in various samples).

The most important point of divergence of our results and conclusions from those of Wilson concerns the band at 1783 cm.$^{-1}$ in the hydride. Our spectra indicate that this band shifts on deuteration to 1290 cm.$^{-1}$, the ratio of frequencies being 1·38. There is no indication that any band of higher frequency shifts on deuteration. Hence we may conclude that the 1783 cm.$^{-1}$ band is due to a vibrational mode involving hydrogen. If the hydrogen is bound closely to the metal atom, as seems probable,[7-9] then this mode is most reasonably assigned as an Mn–H stretching vibration. In the only other carbonyl hydride studied, cobalt tetracarbonyl hydride,[7,10] the highest frequency observed to shift on deuteration, and thus assigned to a mode involving appreciable motion of the hydrogen atom, is that at 703 cm.$^{-1}$; it may be noted, however, that the manganese carbonyl hydride is considerably more stable thermally and chemically than is the cobalt compound, and the metal–hydrogen bond may reasonably be assumed to be stronger.

According to Wilson, the band at 361 cm.$^{-1}$ in the spectrum of the hydride is shifted to 326 cm.$^{-1}$ in that of the deuteride, the ratio of frequencies being 1·11; two more shifts in the middle-frequency region are from 730 to 674 (1·08) and from 612 to 518 (1·18). We find, however, that some rather unusual intensity changes accompany the latter. The region 400—750 cm.$^{-1}$ was carefully studied, the best sample of the deuteride [$\leqslant$5% of the hydride] being used, and the relative intensities reported in Table 2 were calculated from plots of $(\log I_0/I)/lp$ against wavenumber (cm.$^{-1}$), where l, the cell length, was 10 cm., and p, the sample pressure, was 20 mm. for both hydride and deuteride. The band at 453 $\pm$ 2 cm.$^{-1}$ appears to be independent of isotopic substitution and has therefore been used as the reference of intensities in Table 2.

TABLE 2. *Relative intensities of principal peaks in the range* 400—750 *cm.*$^{-1}$.

$HMn(CO)_5$		$DMn(CO)_5$		$HMn(CO)_5$		$DMn(CO)_5$	
cm.$^{-1}$	Rel. intensity	cm.$^{-1}$	Rel. intensity	cm.$^{-1}$	Rel. intensity	cm.$^{-1}$	Rel. intensity
454	1	452	1	{658 / 668}	1·22	{~650 / ~670}	2·55
—	—	511	0·14				
610	1·33	606	0·17	730	1·61	726	0·43

The following explanation of the frequency shifts and concomitant intensity changes is proposed. In manganese pentacarbonyl deuteride there is a weak band at ~511 cm.$^{-1}$ and a strong one at ~670 cm.$^{-1}$ of the same symmetry species (say X) and there are bands at 650—660, ~670, and ~726 cm.$^{-1}$, all of symmetry species other than X. The weak band at 511 cm.$^{-1}$ in the deuteride is shifted up in the hydride so that it becomes degenerate or nearly so with the strong band of species X at about 670 cm.$^{-1}$. Strong, first-order coupling between the two causes the appearance of two bands of comparable intensities at ~730 and 610 cm.$^{-1}$. The peak observed at ~606 cm.$^{-1}$ in the spectrum of the deuteride is thus considered to be due solely to the hydride in our sample. Since the intensity of the band at ~726 cm.$^{-1}$ observed in our deuteride sample did not decrease relative to the

[7] Cotton and Wilkinson, *Chem. and Ind.*, 1956, 1305.
[8] Cotton, *J. Amer. Chem. Soc.*, 1958, **80**, 4425.
[9] Bishop, Down, Richards, and Wilkinson, unpublished work.
[10] Edgell, Magee, and Gallup, *J. Amer. Chem. Soc.*, 1956, **78**, 4185.

730 cm.$^{-1}$ band in the hydride as much as did the ~606 cm.$^{-1}$ band relative to the ~610 cm.$^{-1}$ band in the hydride, we believe that both hydride and deuteride have a band of medium to weak intensity and of symmetry species other than X at ~726 cm.$^{-1}$. The ratio (RD/RH) of the total intensity of the shifted bands in the deuteride to that of their counterparts in the hydride is difficult to estimate accurately owing to overlapping with isotope-independent bands, but is 0·6—0·8, which is qualitatively to be expected. We are thus in superficial agreement with Wilson as to his reported 730—674 cm.$^{-1}$ and 612—518 cm.$^{-1}$ shifts, but believe that the relations are more complicated than his discussion implies when the intensity changes are considered.

Whether the molecular symmetry of manganese pentacarbonyl hydride is C_{2v} or C_s, it appears that there must still be other bands of the same symmetry species as the 361 cm.$^{-1}$ band which are appreciably shifted upon deuterium substitution. The internal co-ordinates of the hydrogen atom must contribute to three symmetry co-ordinates, which, in the case of C_{2v} symmetry, would all be of different symmetry classes. For each of these there should be a set of bands whose shift ratios when multiplied together give a product a little less than 1·41, according to the Teller–Redlich theorem (and allowing for the effects of translations and anharmonicities). The 1785—1290 shift can, by itself, be one of these sets (ratio ~1·38) and the two shifts 730—670 and 610—511 with a product of ratios of ~1·30 can account for most of a second. The shift 361—326 (ratio 1·11) reported by Wilson would seem therefore to be a contributor to the product of shift ratios in a third set, since both $1{\cdot}30 \times 1{\cdot}11 = 1{\cdot}43$ and $1{\cdot}38 \times 1{\cdot}11 = 1{\cdot}53$ exceed 1·41. Presumably, one or more shifts of bands belonging to the same symmetry species as the 361 cm.$^{-1}$ band remain to be found, and one may be due to a mode which involves very considerable motion of the hydrogen atom. Such a band or bands probably lie below 300 cm.$^{-1}$. In the case where manganese pentacarbonyl hydride has C_s symmetry the argument is changed in detail but the same conclusion is drawn.

Proton Resonance Spectrum.—The nuclear resonance spectrum at 40 Mc./sec. of manganese pentacarbonyl hydride consists of one line at 519·5 c./sec. (13·0 parts per million) on the high-field side referred to water at 22°. Thus it can be concluded that the proton in the hydride is in an environment qualitatively similar to that of the protons in $HCo(CO)_4$ and $H_2Fe(CO)_4$ for which shifts of $15{\cdot}5 \pm 2{\cdot}0$ [11] and $15{\cdot}6 \pm 0{\cdot}5$ parts per million,[7] respectively, have been observed.

Experimental

Preparation of Samples.—Manganese carbonyl, $Mn_2(CO)_{10}$, was treated with aqueous potassium hydroxide in a nitrogen atmosphere to form a solution of $KMn(CO)_5$. On addition of a slight excess of dilute sulphuric acid the hydride was liberated. It was slowly swept out of the reaction vessel and through a column of calcium chloride with a stream of nitrogen and collected in a trap cooled with solid carbon dioxide. It was then further purified by several trap-to-trap distillations on a vacuum line.

In order to prepare the deuteride, the hydride (prepared as described above) was distilled into a solution of sodium deuteroxide in deuterium oxide and the solution set aside for 12 hr. The deuterium oxide was then pumped off, fresh deuterium oxide (99·5% D_2O) condensed on the solid sodium compound, and the solution stored for several hours. Acidification was with a solution of deuterium chloride in deuterium oxide, prepared by hydrolysis of boron trichloride in deuterium oxide. The deuteride was then swept out with dry nitrogen and subjected to several trap-to-trap distillations to give a product of m. p. ~−21°. Care was taken to dry all apparatus with which manganese pentacarbonyl deuteride came into contact.

Infrared Spectra.—Gaseous samples were examined in 10-cm. cells equipped with potassium bromide windows. Gas pressures were generally of the order of 20—28 mm. except when the intense carbonyl peaks were examined, for which they had to be considerably reduced. The entire spectrum of each compound was studied by using a Perkin-Elmer model 21 double-beam spectrometer with sodium chloride and potassium bromide prisms. The CO stretching region

[11] Gutowsky, quoted by Sternberg *et al.*, *J. Amer. Chem. Soc.*, 1955, **77**, 3951.

was studied with a modified Grubb-Parsons double-beam spectrometer with a lithium fluoride prism.

Special precautions were taken to eliminate water vapour from the cell and auxiliary apparatus when studying the deuteride. The cell was repeatedly treated with deuterium oxide vapour (several times overnight), followed by evacuation, before being filled with the deuteride. In certain cases, as noted in the Discussion, pressures in the cell were measured fairly accurately for comparing intensities of bands in the spectra of the two compounds.

Proton Resonance Spectrum.—The spectrum of the hydride containing a trace of 1 : 2-dimethoxyethane was recorded by using a Varian Associates Model V-4300B high-resolution spectrometer and the conventional techniques. The ether proton line, used as an internal standard, was then referred to water at 22° ± 1°. Measurements were made at 40 Mc./sec.

We thank Professor W. C. Price and Dr. George Wilkinson, of King's College, London, for advice and assistance in obtaining spectra with the lithium fluoride prism, and Professor R. C. Lord, of the Massachusetts Institute of Technology, for valuable discussions.

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168. *High-temperature Thermal Decomposition of Ammonium Perchlorate.*

By A. K. Galwey and P. W. M. Jacobs.

The thermal decomposition of ammonium perchlorate at temperatures above about 350° c differs in several respects from that below this temperature. Reaction occurs by a different mechanism and here results in complete decomposition, whereas at low temperatures a residue of ammonium perchlorate always remains. Results for the kinetics of the high-temperature reaction have been analysed according to two alternative equations. Both fit the results well, but one of them, the "contracting-cube" formula, is preferred on theoretical grounds. A mechanism of the high-temperature reaction, consistent with that for the low-temperature reaction, is proposed.

Bircumshaw and Newman [1] made a brief study of the thermal decomposition of ammonium perchlorate in the temperature range 380—450°, sublimation of the reactant from the hot zone being prevented by a small pressure of inert gas. They noted that the reaction obeys the power law

$$p = kt^n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where p is the pressure evolved in a constant-volume system in time t, and k and n are constants. The exponent n varied somewhat irregularly with temperature between 0·5 and 1·0. The reaction was deceleratory throughout and, in contrast to the low-temperature decomposition, resulted in complete decomposition of the salt.

After this work had been completed, Bircumshaw and Phillips [2] reported that between 300° and 380° the thermal decomposition of ammonium perchlorate gave irreproducible kinetic results under a wide variety of conditions, but reproducible ones from decompositions at 400—440°, velocity constants being dependent on the pressure of nitrogen used to suppress sublimation. The kinetics of the high-temperature decomposition fitted the equation $m^{2/3} = kt + c$, where m is the mass of salt undecomposed at time t, and k

[1] Bircumshaw and Newman, *Proc. Roy. Soc.*, 1954, *A*, **227**, 115; 1955, *A*, **227**, 228.
[2] Bircumshaw and Phillips, *J.*, 1957, 4741.

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and c are constants. Sublimation was prevented by a pressure of 20 cm. of nitrogen and an energy of activation of $73{\cdot}4 \pm 1{\cdot}5$ kcal./mole was obtained from the dependence of the rate constant (k) on temperature. Decomposition was virtually complete, and the gaseous products did not catalyse the reaction. Bircumshaw and Phillips suggested that the rate-determining step in the high-temperature reaction is the breakdown of the perchlorate ion because the energy of activation found was similar to that for the decomposition of pure potassium perchlorate (63·3 kcal./mole).[3]

The decomposition of ammonium perchlorate below 350° will be discussed in detail elsewhere [4] (see also refs. 1, 2, 3); the essential feature is that only intergranular material is decomposed, leaving a residue of salt chemically identical with the starting material.

Experimental

The apparatus used [4] to study the low-temperature decomposition is unsuitable at high temperatures because it was necessary to introduce an inert gas before each experiment and it was not possible to take a sufficient number of McLeod gauge readings to characterise the kinetics in runs lasting less than about 2 hr. Accordingly an apparatus was developed in which the pressure was measured by means of a glass spiral manometer. The pressure developed during decomposition in a constant-volume system was measured by the deflection (θ) of a light spot, reflected from a mirror mounted on the glass spiral on to a fixed scale. Calibration of this gauge, using a mercury manometer, showed that θ is proportional to the pressure difference across the gauge spiral and independent of the absolute pressure in the apparatus. Pressure readings could be taken every 10 sec., with an accuracy $\pm 0{\cdot}05$ mm. Hg.

Preparation of materials will be described elsewhere.[4]

Results

In the high-temperature decomposition region (above 350°) sublimation is fast. The behaviour of the salt at 350° in the presence and absence of inert gas is shown in Fig. 1. Curve A shows the variation of pressure with time observed for the decomposition of a fragment of a

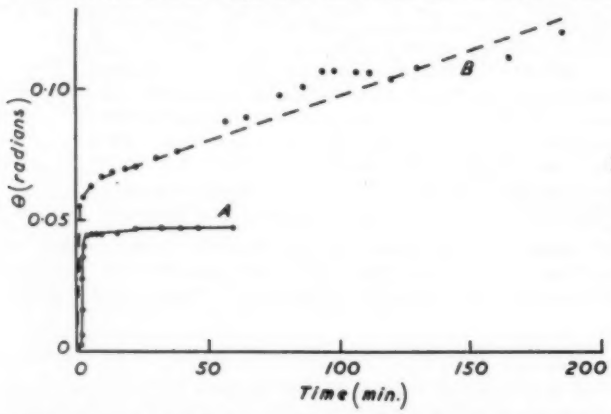

Fig. 1. *Pressure–time plots for the thermal decomposition of ammonium perchlorate pellet fragments* in vacuo (A) *and in* 400 *mm. of gas* (B).

pellet dropped into the hot zone *in vacuo*. There was no residue, but substantial sublimation to the cooler walls above the reaction zone had occurred. In a similar run B with a pellet of nearly equal mass and the tube filled with 400 mm. of gas to suppress sublimation the fast initial pressure rise was followed by a slow rise in pressure. After 6 hours, while the slow reaction was still proceeding, only about one-third of the original weight of sample remained and no visible sublimation had occurred.

As Bircumshaw and Phillips [3] report, the kinetics in the range 300—380° are irreproducible, though the low-temperature thermal decomposition *in vacuo* gave satisfactory rate constants up to 350°. Reactions in the presence of an inert gas were irreproducible at this temperature

[3] Phillips, Thesis, Birmingham, 1953 (quoted in ref. 2).
[4] Galwey and Jacobs, to be published.

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and probably consist of a mixture of the low-temperature decomposition and the reaction seen to occur when sublimation is suppressed, which will be called the high-temperature reaction.

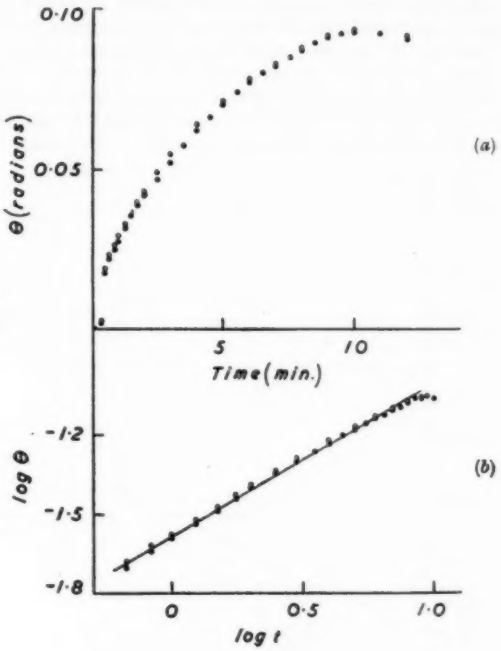


FIG. 2. *Thermal decomposition of pellet fragments of ammonium perchlorate at 407°. Full and open circles refer to two runs under identical conditions.*

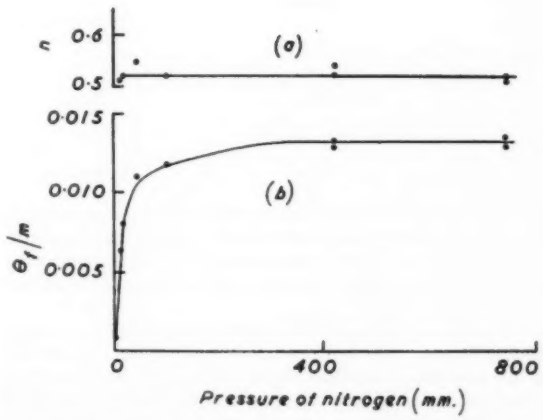


FIG. 3. *Thermal decomposition of ammonium perchlorate pellet fragments at 407°. Plots of (a) power-law index (n) and (b) ratio of final pressure to weight taken (θ_f/m), against the pressure of nitrogen used to suppress sublimation.*

Reproducibility.—Decompositions above 380° were reproducible. Three fragments of a single pellet of ammonium perchlorate, having very nearly equal masses, decomposed in 20 mm. of nitrogen under identical conditions to give virtually identical pressure–time curves. Two of these runs are represented in Fig. 2*a*, the third being omitted for clarity. These plots are deceleratory throughout, a characteristic feature of the high-temperature reaction. Fig. 2*b* shows the plot of log θ against log t for the same runs; the power law holds satisfactorily over the greater part of the reaction with $n = 0{\cdot}57$.

Variation of Pressure of Gas used to suppress Sublimation.—Successive fragments of a single

pellet, of approximately equal masses, were decomposed at the same temperature under different initial pressures of dry nitrogen. The results, summarised in Fig. 3, show that the power law is obeyed, n being independent of the pressure of nitrogen, and that at low initial pressures, where substantial sublimation occurred, the ratio of the final pressure evolved as a result of decomposition (θ_f) to weight of sample (m) is small but increases rapidly with initial pressure of nitrogen. θ_f/m may be taken as a measure of the extent of reaction in this system where sublimation is fast; it is nearly independent of nitrogen pressure above about 300 mm., and 400 mm. was therefore used, unless otherwise stated.

Variation of Mass of Pellet.—Successive fragments of different mass of a single pellet were decomposed under identical conditions. The range of mass is limited by the sensitivity of the

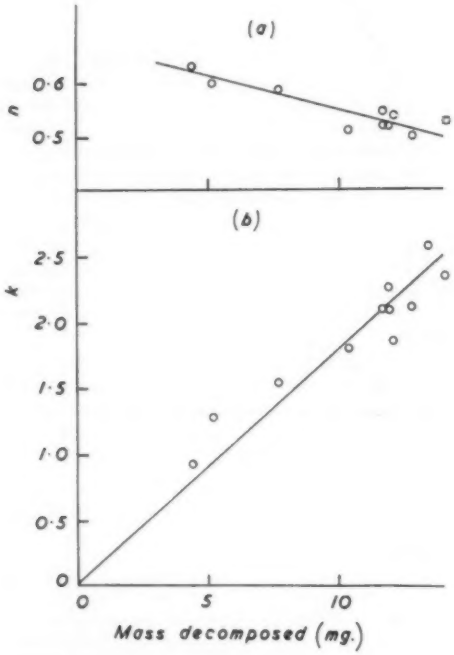


FIG. 4. *Thermal decomposition of ammonium perchlorate pellet fragments at 407° in 400 mm. of nitrogen. Variation of (a) power-law index (n) and (b) power-law rate constant (k) with mass decomposed.*

gauge at one extreme, and the largest mass which could be decomposed without causing condensation of water vapour, at the other. The results (Fig. 4) show that n varies somewhat with the mass decomposed, and that the rate constant is directly proportional to the mass decomposed. Attempts to fit the results to the Prout–Tompkins equation and to the unimolecular-decay law failed.

Variation of Temperature.—Pellets. Successive fragments of nearly equal mass of a single pellet were decomposed at different temperatures. All the pressure–time curves showed the characteristic shape illustrated in Fig. 2*a* and the power law fitted the results well over the whole reaction period in several runs. In certain runs, however, the index n was not constant throughout the reaction and two values, holding over different stages were found; a run showing this is in Fig. 5*a*. A plot of power-law indices against temperature of decomposition is shown in Fig. 5*b*. At lower temperatures, in the range studied, two different reaction periods are observed. Both indices increase with temperature, that for the initial period increasing more quickly than that for the decay period so that at higher temperature only a single value of the exponent is required.

Arrhenius energies of activation for the reaction were determined from plots of log (k/m) against $1/T°$ (K); log (k/m) was used since $k \propto m$, although the variation in mass for runs of this series was minimised. The plot for the initial region of reaction was too scattered to yield an

energy of activation, but a satisfactory plot for the decay period was obtained. This is well represented by the equation:

$$\log (k/m) = 4{\cdot}96 - 17{,}540/(2{\cdot}303\boldsymbol{R}T)$$

which is valid for $0{\cdot}26 < \alpha < 0{\cdot}92$, m being expressed in mg. For three runs 400 mm. of oxygen was used instead of nitrogen. The rate constants and power law indices (Fig. 5*b*) are independent of which gas was used.

Single whole crystals. Single whole crystals, all prepared in a single recrystallisation, were decomposed under similar conditions to those used for pellets. The results fitted the power

FIG. 5. *Thermal decomposition of ammonium perchlorate pellet fragments. (a) Pressure–time plot in the temperature region where two different values of the rate constant hold. (b) Variation of n with temperature of decomposition: broken line initial region; full line, final region. Open circles represent runs in an atmosphere of oxygen; other runs in nitrogen.*

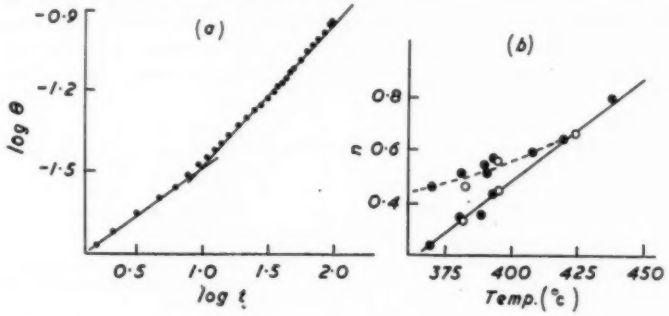


FIG. 6. *Thermal decomposition of ammonium perchlorate pellets previously decomposed at low temperatures. Plot of* log θ versus log t *showing three regions of reaction (θ in radians, t in minutes).*

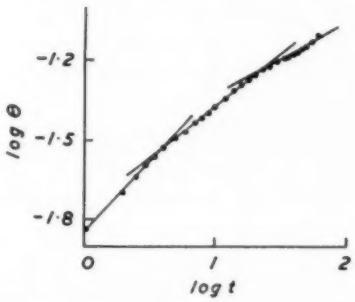
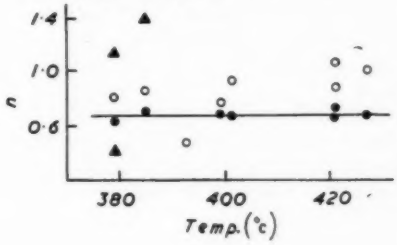


FIG. 7. *Thermal decomposition of ammonium perchlorate pellets previously decomposed at low temperatures*: ▲ initial region; ○ middle region; ● final region.



law although there was a perceptible curvature of the log p–log t plot, and results were less reproducible than those for pellet fragments. An Arrhenius plot was too scattered to yield an energy of activation. The values of n showed some scatter, but no systematic variation with temperature.

Residue from low-temperature thermal decompositions. Since reaction goes to completion in the high-temperature region it was clearly important to study, in this temperature range, the decomposition of residue left from the low-temperature thermal decomposition. Accordingly the materials from pellet fragments decomposed at 250—350° were reheated in the high-temperature range after being stored over fresh phosphoric oxide for not more than three days (usually not more than one day). Great care was taken to avoid mechanical damage and to limit contact with the atmosphere.

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Here the power law was less satisfactory. In Fig. 6, three reaction regions are characterised by different rate constants and different exponents, though in some other runs of this series only two can be distinguished. Plots of the power-law indices for the middle (n_b) and final (n_c) regions of reaction show scatter, but no definite trend with temperature (Fig. 7). Arrhenius plots with rate constants for the middle (k_b) and final (k_c) regions were well represented by the equations:

$$\log (k_b/m) = 8{\cdot}67 - 30{,}000/(2{\cdot}303\boldsymbol{R}T), \quad 0{\cdot}15 < \alpha < 0{\cdot}40$$

$$\text{and} \quad \log (k_c/m) = 8{\cdot}77 - 30{,}000/(2{\cdot}303\boldsymbol{R}T), \quad 0{\cdot}43 < \alpha < 0{\cdot}95.$$

Discussion

The results for the high-temperature thermal decomposition of ammonium perchlorate fit the power law over a wide range of α. The fit is particularly satisfactory for the decomposition of "undecomposed" ammonium perchlorate; for several runs the equation holds over the complete reaction, the power-law index and rate constants being accurately reproducible. The power law, taken as an empirical equation, is useful for describing and systematising the experimental results. There are, however, theoretical objections to its use.

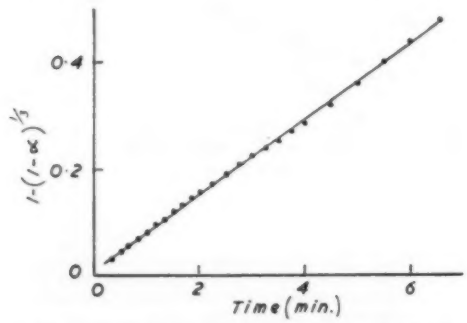

Fig. 8. *Thermal decomposition of a pellet of ammonium perchlorate: test of the contracting-cube formula.*

The power-law index varies with both the mass of fragment and the temperature of decomposition. The actual n–m and n–T relationships could not be expressed analytically owing to scatter (Figs. 4*a* and 5*b*) but the variability of n makes the significance of the derived energy of activation doubtful since the rate constants (given by $\log p$ when $\log t = 0$) depend on the slope of the $\log p$–$\log t$ plot, that is, on the value of n.

In several runs the power law shows more than one region of reaction, different values of n and k holding over successive ranges of α, the fractional decomposition, *e.g.*, Fig. 6. Also, the equation can only be regarded as fitting approximately the results for decomposition of whole crystals.

Finally, it is difficult to account for an exponent of less than unity in applying the power law to the decomposition of a solid. A value of $n < 1$ could be due to decomposition in the gas phase following sublimation of the solid, but the experimental evidence (Fig. 1) is that sublimation and decomposition are competing processes.

The first reaction, after the sample had been placed in the furnace (>350°), must involve the material which can decompose at low temperature, that is, the strained, intergranular regions of the lattice.[4] This leaves a residue consisting of a large number of blocks of material, adhering loosely at corners and edges. Their decomposition should obey an equation based on the recession of an interface parallel to the particle surface, that is, the contracting-cube formula:

$$kt = 1 - (1 - \alpha)^{\frac{1}{3}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

To test this conclusion, the results were re-analysed by plotting $[1 - (1 - \alpha)^{\frac{1}{3}}]$ against t (Fig. 8). For pellets, decomposed and undecomposed, rate constants hold over the

approximate range $0{\cdot}2 < \alpha < 0{\cdot}8$ and for crystals $0 < \alpha < 0{\cdot}7$. An Arrhenius plot for the decomposition of pellet fragments only, with rate constants derived from eqn. (2), yields an energy of activation of 38·8 kcal./mole.

Eqn. (2) requires that $1 - (1 - \alpha)^{\frac{1}{3}} = 0$ when $t = 0$, but the best experimental straight line did not always pass through the origin. This could be due either to initial rapid decomposition (the low-temperature reaction) or to a finite heating time or to a combination of both factors.

A composite Arrhenius plot for rate constants found by using eqn. (2) for the thermal decomposition of fragments of undecomposed ammonium perchlorate, fragments of ammonium perchlorate pellet which has undergone low temperature thermal decomposition, and whole single crystals of ammonium perchlorate, is shown in Fig. 9. The

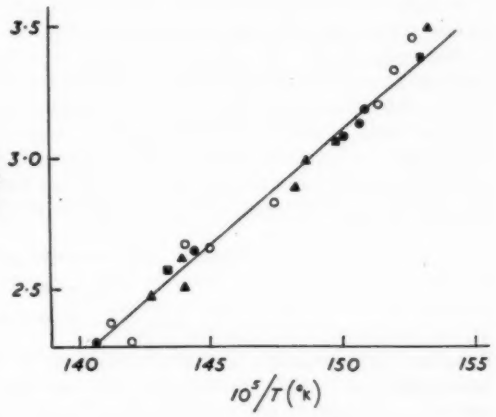

FIG. 9. *Arrhenius plot for the thermal decomposition of ammonium perchlorate. Fragments of a pellet of normal salt in nitrogen (●) and in oxygen (■). ▲, Pellet fragments previously decomposed at low temperatures; ○, single whole crystals.*

line gives the best fit for decomposition of fragments of undecomposed pellet, the plot for this series showing the least scatter of the three materials investigated. All the points lie reasonably close to the single straight line. Thus a *single* kinetic equation is obeyed over a large fraction of the decomposition for all three forms. The difficulty of theoretically accounting for the variation of power-law index with fragment mass and temperature does not arise with the contracting-cube law.

Since reaction above about 380° goes to completion for all three forms and the kinetic equations obeyed in the high- and the low-temperature range are quite different, different processes must control the rate.

Two possible reaction mechanisms are consistent with the contracting-cube model: (i) evaporation of an ion-pair followed by gas-phase decomposition of the ammonium perchlorate; (ii) proton transfer on the solid surface giving ammonia and perchloric acid.

In the high-temperature range, decomposition and sublimation probably compete since ammonium perchlorate can sublime unchanged *in vacuo*; the decomposition observed (Fig. 1) under these conditions can be attributed to the low-temperature reaction (which is independent of sublimation in the low-temperature range [1]). The mechanism by which ammonium perchlorate sublimes has not been established experimentally, but the volatile species in sublimation is probably an ion-pair formed as a result of the powerful proton-donating power of perchloric acid and stabilised by hydrogen-bonding. Ammonium salts of weaker acids sublime through dissociation (*e.g.*, $NH_4Cl \longrightarrow NH_3 + HCl$) but this may not occur with the ammonium salt of so strong an acid. The increased stability of perchloric acid to heat resulting from hydration gives further evidence for the existence

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of complexes of the acid capable of existence as gases, since the pure acid decomposes at 92° whereas an acid of composition $HClO_4,2H_2O$ distils at 203°.[5]

Energies of activation for sublimation and decomposition can be compared only if derived by use of the same kinetic equation or referred specifically to the same process (*e.g.*, propagation of an interface). Bircumshaw and Phillips [2] found the energy of activation for the sublimation to be 21·5 ± 2·78 kcal./mole using rate constants deduced from the equation $dm/dt = k$, which is the power law with an index of unity. This value cannot be compared with results for decomposition of fragments of fresh pellets since the power-law index varies systematically with temperature. However, comparison may be made with the energy of activation (30 kcal./mole) deduced from the power-law rate-constants found for the middle region of reaction of " decomposed " pellets where the exponent is approximately 0·9 and does not vary systematically with temperature. The large difference between the two energies of activation implies that different rate-determining steps operate in sublimation and high-temperature decomposition.

We suggest that the rate-determining step for the high-temperature thermal decomposition is a proton-transfer on the surface of the solid followed by oxidation of the ammonia gas by radicals resulting from the decomposition of perchloric acid. The mechanism of decomposition of perchloric acid has not yet been established, though the liquid decomposes below 100°, a reaction attributed [5] to the instability of the anhydride Cl_2O_7. It seems probable that perchloric acid should undergo fast decomposition at these temperatures, generating oxygen atoms which then oxidise the ammonia:

$$2HClO_4 \longrightarrow H_2O + Cl_2O_7 \quad \ldots\ldots\ldots\ldots \quad (3)$$

$$Cl_2O_7 \longrightarrow 2Cl_2 + 7O_2 \quad \ldots\ldots\ldots\ldots \quad (4)$$

$$4NH_3 + 5O_2 \longrightarrow 6H_2O + 4NO \quad \ldots\ldots\ldots\ldots \quad (5)$$

Reaction (4) is probably a chain reaction involving ClO_4, ClO_3, ClO_2, ClO, Cl, and O as intermediates.[6,7] The mechanism for the homogeneous oxidation of ammonia by molecular oxygen is not established in detail but the reaction is slow below 500°,[8] so that the oxidation of ammonia at these temperatures must be by atomic oxygen, from the decomposition of Cl_2O_7. This scheme accounts for the major products found by Dodé [9] who represented the overall reaction by

$$2NH_4ClO_4 \longrightarrow 4H_2O + 2NO + O_2 + Cl_2$$

The appearance of nitrosyl chloride and nitrogen as minor products is accounted for by the reaction of NO with Cl and the combination of N atoms [formed in eqn. (5)], respectively. The details of the reaction cannot yet be established, but our scheme accounts for the products and is consistent with known facts.

We thank Dr. W. G. Parker, of R.A.E., Westcott, and Mr. G. K. Adams and Dr. J. Powling of E.R.D.E., Waltham Abbey, for interest and encouragement.

IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, September 8th*, 1958.]

[5] Ephraim, " Inorganic Chemistry," 5th Edn., Gurney and Jackson, London, 1948, p. 389.
[6] Figini, Colloccia, and Schumacher, *Z. phys. Chem.*, 1958, **14**, 32.
[7] Schumacher and Stieger, *Z. phys. Chem.*, 1930, *B*, **7**, 363.
[8] Stephens and Pease, *J. Amer. Chem. Soc.*, 1950, **72**, 1188; 1952, **74**, 3480.
[9] Dodé, *Bull. Soc. chim. France*, 1938, **5**, 170.

169. *Acetyl Chloride as a Polar Solvent. Part V.*[1] *Titrations in Acetyl Chloride.*

By Jaswant Singh, Ram Chand Paul, and Sarjit Singh Sandhu.

Following studies of the polar behaviour of acetyl chloride[1] we have attempted acid–base titrations in that solvent in the presence of indicators. Crystal Violet and benzanthrone were used as indicators which are not reacted upon irreversibly by acetyl chloride.

Crystal Violet has been used in the study of acid–base neutralizations in thionyl chloride,[2] but results were unsatisfactory as the indicator is unstable therein. In acetyl chloride, however, its colour changes are reversible and the dye is sufficiently stable. The colours of Crystal Violet and benzanthrone in acetyl chloride and in the solutions of solvoacids and solvobases in acetyl chloride are recorded in Table 1.

Table 1. *Colours in acetyl chloride and in acetyl chloride solutions of various solutes.*

Indicator	Concn.	None	$TiCl_4$	$SnCl_4$	quinoline	α-picoline	$Ph{\cdot}NMe_2$
Crystal Violet	moderate	blue	deep yellow	yellow	violet	violet	pink
	high	—	orange yellow	orange yellow	purple	purple	blue
Benzanthrone	moderate	yellow	deep red	red	yellow	yellow	light yellow
	high	—	blood red	deep red	deep yellow	deep yellow	light yellow

The colour changes of Crystal Violet are therefore in the same order in the presence of acids and bases in acetyl chloride as in water, for in aqueous solutions Crystal Violet is yellow, green, and violet at pH 0·1, 1·5, and 3·2, respectively.[3] Similar colour changes in acetic acid have also been reported.[4] The blue colour of Crystal Violet in acetyl chloride serves as a test for the latter's purity for if traces of hydrochloric acid and acetic acid are present the solutions become green and finally yellow. In concentrated sulphuric acid benzanthrone yields a red colour which changes to yellow on large dilution or in the presence of alkalis.

In these acid–base neutralizations in acetyl chloride, precipitation makes detection of colour change near the end point difficult. This has been surmounted by adding the solution dropwise and, on appearance of any colour change, allowing the precipitate to settle before the colour of the supernatant liquid is noted. To examine the reversibility of the indicator, in one set of experiments acid solutions were titrated and in the other the base. Each titration was in duplicate. Results are presented in Table 2.

The colour of Crystal Violet at the neutralization point depends on the individual acid–base pair and the difference is presumably related to the relative strength of the acids and bases in acetyl chloride.[5] For instance, the yellow colour at the neutralization point of dimethylaniline with both acids indicates that dimethylaniline is a weaker base than quinoline and this observation is supported by the colour of Crystal Violet in solutions of quinoline and dimethylaniline in acetyl chloride (Table 1). The values of specific conductivity[3] of these solvobases in acetyl chloride support this observation. The absence of green colour at the neutralization point of dimethylaniline recalls the neutralization of a weak base such as ammonia with hydrochloric acid or sulphuric acid in aqueous solution. The acid colour of the indicator at the neutralization point is explained by hydrolysis of the salts of weak bases and strong acids in aqueous solutions; presumably the yellow colour at the neutralization point of dimethylaniline with stannic chloride is related to the former's weakly basic character.

[1] Part IV, *J.*, 1959, 325.
[2] Garber, Pease, and Luder, *Analyt. Chem.*, 1953, **25**, 581.
[3] Rice, Zuffanti, and Luder, *ibid.*, 1952, **24**, 1022.
[4] Seaman and Allen, *ibid.*, 1951, **23**, 592.
[5] Hawke and Steigman, *ibid.*, 1954, **26**, 1989.

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TABLE 2.

Titrant	Reagent	[Titrant]	Vol. of titrant (ml.) (Used)	Vol. of titrant (ml.) (Calc.)	Colour at end point
		Crystal Violet			
Quinoline	Stannic chloride	0·1345	2·30	2·41	Green
	Titanium tetrachloride	0·1298	1·21	1·37	Green
α-Picoline	Stannic chloride	0·1142	18·40	18·24	Greenish yellow
	Titanium tetrachloride	0·2094	5·70	5·70	Greenish yellow
Dimethylaniline	Stannic chloride	0·1352	1·40	1·37	Pale yellow
	Titanium tetrachloride	1·3352	5·20	4·59	Pale yellow
Stannic chloride	Quinoline	0·0788	16·10	16·07	Greenish yellow
	α-Picoline	0·0883	7·85	7·73	Yellow
	Dimethylaniline	0·6277	8·40	8·61	Yellow
Titanium tetrachloride	Quinoline	0·0597	5·00	4·55	Greenish yellow
	α-Picoline	0·0342	8·50	8·49	Yellow
	Dimethylaniline	0·0442	4·80	4·91	Yellow
		Benzanthrone			
Quinoline	Stannic chloride	0·0885	2·90	2·59	Yellow
	Titanium tetrachloride	0·0885	6·00	6·10	Yellow
α-Picoline	Stannic chloride	0·1478	6·10	6·09	Yellow
	Titanium tetrachloride	0·1478	16·40	16·31	Yellow
Dimethylaniline	Stannic chloride	0·0836	3·60	3·72	Pale yellow
	Titanium tetrachloride	1·2180	4·20	4·32	Yellow
Stannic chloride	Quinoline	0·0806	5·05	5·10	Orange red
	α-Picoline	0·1086	2·90	2·77	Orange yellow
	Dimethylaniline	0·0806	2·20	2·04	Orange
Titanium tetrachloride	Quinoline	0·0875	3·05	3·15	Orange red
	α-Picoline	0·0875	5·50	5·41	Orange yellow
	Dimethylaniline	0·0875	3·50	3·55	Orange yellow

The appearance of different colours at the theoretical neutralization point of different pairs of acids and bases suggests that the orders of relative strength in acetyl chloride are: stannic chloride > titanium tetrachloride; quinoline > α-picoline > dimethylaniline. Surprisingly, the order of strength of the bases is different in aqueous solutions as the following pK_a values [6] show: dimethylaniline 5·06, α-picoline 5·05, quinoline 4·85. This anomaly can, however, be explained by comparison of the steric requirements of the acetylium ion and the proton.

Benzanthrone differs from Crystal Violet in that it does not show a gradation of colour. It cannot therefore be used to arrange acids and bases according to their strengths. This may be due to a large value of the transition interval of benzanthrone or to benzanthrone's showing only two colours, one in acidic and one in basic solutions in acetyl chloride.

Attempts to use carbon tetrachloride in these titrations were unsuccessful.

The colour changes of these indicators can be explained on the basis of the existence (already postulated [1]) of ionic species in acetyl chloride solutions. The solvoacids stannic chloride and titanium tetrachloride dissolve in acetyl chloride and increase the concentration of acetylium ions (which correspond to the hydrogen ions of aqueous solutions), *e.g.*,

$$SnCl_4 + 2AcCl \rightleftharpoons 2Ac^+ + SnCl_6^{2-}$$

Solvobases ionize in acetyl chloride and similarly bring about an increase in the concentration of chloride ions.

Experimental.—A burette equipped with reservoir for stock solution of the titrant connected to a titration bottle and an arrangement for magnetic stirring was employed. The apparatus was guarded from moisture by freshly prepared calcium chloride.

The acids and bases were weighed by difference and care was taken to avoid the contact of moisture. 20 ml. of the solvent were taken in the titration bottle and a weighed amount of the substance to be titrated was added. The indicator (3—5 mg.) was added, and the

[6] Braude and Nachod, "Determination of organic structures by physical methods," Academic Press Inc., New York, N.Y., 1955, pp. 600, 613.

mixture was stirred magnetically. The titrant solutions were prepared in a 100-ml. measuring flask in a dry box. Burette readings were noted corresponding to changes in colour of the indicator; the results are given in Table 2. The volume of titrant recorded is that of the colour change nearest the expected end-point.

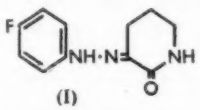
PANJAB UNIVERSITY, HOSHIARPUR, INDIA. [*Received, June 20th*, 1958.]

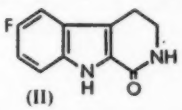
170. 5-*Fluorotryptamine.*

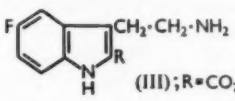
By Z. PELCHOWICZ and ERNST D. BERGMANN.

THE interesting biological properties of 5-fluorotryptophan made it desirable to prepare 5-fluorotryptamine (IV) both as analogue of tryptamine and serotonine and as starting material for further syntheses. The synthesis was based on previous observations.[1]

Ethyl 2-oxopiperidine-3-carboxylate and *p*-fluorobenzenediazonium chloride gave in 56% yield 2 : 3-dioxopiperidine *p*-fluorophenylhydrazone (I), which was cyclized by acid to the carboline II (yield, 71%). This was hydrolyzed to 5-fluorotryptamine-2-carboxylic acid (III) in 85% yield and the latter decarboxylated to the tryptamine (IV) (best isolated in form of its stable hydrochloride). The overall yield was 29%.


(I)


(II)


(III); R = CO_2H. (IV); R = H

Given subcutaneously to mice, 5-fluorotryptamine (LD_{50} 439 mg./kg.) is more toxic than serotonine (>868 mg./kg.),[2] whilst intracerebrally the tryptamine induced central effects similar to 10—30 μg. of serotonin [3] only in doses above 250 μg. per mouse. A full report on the toxicological properties of 5-fluorotryptamine will be published elsewhere by Dr. H. Edery.

Experimental.—2 : 3-*Dioxopiperidine* 3-*p-fluorophenylhydrazone* (I). To a well-agitated solution of ethyl 2-oxopiperidine-3-carboxylate [4] (47 g.) and potassium hydroxide (16·5 g.) in water (550 ml.), which had been kept at room temperature for 24 hr., filtered, and cooled to 0°, was added a solution of *p*-fluorobenzenediazonium chloride [from 4-fluoroaniline [5] (32·1 g.). After 5 min., the product was adjusted to pH 3—4 (acetic acid) and then stirred for 5 hr. at 5°. Filtration gave the *derivative* (I) (37 g.; 56%), which crystallized from methanol in yellow needles, m. p. 214·5—215° (Found: C, 59·9; H, 5·3; F, 8·9. $C_{11}H_{12}ON_3F$ requires C, 59·7; H, 5·5; F, 8·6%).

6-*Fluoro*-1 : 2 : 3 : 4-*tetrahydro*-1-*oxo*-β-*carboline* (II).—A mixture of (I) (26 g.), concentrated hydrochloric acid (60 ml.), and acetic acid (120 ml.) was refluxed for 3 hr. The crystals which separated upon cooling, and a second crop which was precipitated by addition of water to the filtrate, were recrystallized from aqueous alcohol; the *crystals* (17 g.; 71%) had m. p. 236—237° (Found: C, 64·8; H, 4·7; F, 9·7. $C_{11}H_9ON_2F$ requires C, 64·6; H, 4·5; F, 9·3%).

5-*Fluorotryptamine*-2-*carboxylic acid* (III). A mixture of the carboline (II) (15 g.), dissolved in alcohol (150 ml.), and potassium hydroxide (33·5 g.), dissolved in water (150 ml.), was refluxed for 1 hr. Then 150 ml. of the liquid were distilled off and replaced by the same quantity of water. The solution was cooled, decolorized with active charcoal, filtered, and acidified with acetic acid. After recrystallization from water, the crystals (14 g.; 85%) melted at 285—287° (decomp.) (Found: C, 59·3; H, 5·2; F, 8·6. $C_{11}H_{11}O_2N_2F$ requires C, 59·4; H, 5·0; F, 8·6%).

[1] Japp and Klingemann, *Ber.*, 1887, **20**, 2942, 3284, 3398; *Annalen*, 1888, **247**, 218; Shapiro and Abramovitch, *Chem. and Ind.*, 1955, 1255; *J. Amer. Chem. Soc.*, 1955, **77**, 6690; *J.*, 1956, 4589; Henecka, Timmler, Lorenz, and Geiger, *Ber.*, 1957, **90**, 1060; Quadbeck and Rohm, *Z. physiol Chem.*, 1954, **297**, 229.

[2] Freyburger, *J. Pharm. Exp. Ther.*, 1952, **105**, 80.

[3] Haley, *Acta Pharmacol. Toxicol.*, 1957, **13**, 107.

[4] Albertson and Fillman, *J. Amer. Chem. Soc.*, 1949, **71**, 2819.

[5] Bradlow and VanderWerf, *ibid.*, 1948, **70**, 654.

5-Fluorotryptamine hydrochloride (IV). A mixture of the carboxylic acid (6 g.) and 10% hydrochloric acid (180 ml.) was refluxed until the evolution of gas ceased and a clear solution had formed. Upon cooling, crystals (5 g.; 86%) separated, which were recrystallized by adding ether to their alcoholic solution; they melted at 282° (Found: C, 56·0; H, 5·6. $C_{10}H_{12}N_2ClF$ requires C, 56·1; H, 5·6%).

SCIENTIFIC DEPARTMENT, MINISTRY OF DEFENCE, TEL-AVIV. [*Received, July 7th*, 1958.]

171. *The Extractives of* Quintinnia serrata.

By R. C. CAMBIE.

Quintinnia serrata A. Cunn. (New Zealand " Tawheowheo ") is a tree which is endemic and common in forests of the North Island of New Zealand. Extraction of the dried bark with aqueous methanol gave a crystalline phenolic glucoside (12·5% yield), circular R_F 0·17, with traces of a further phenolic non-glycosidic constituent, circular R_F 0·74. The latter was identified by paper chromatography as dihydroquercetin, after separation from the total solid by ether-extraction. The ether-insoluble glycoside was a dextrorotatory rhamnoside of (±)-dihydroquercetin, the melting point of which (179·5°) agreed with that recorded for the 3-rhamnoside, astilbin.[1,2] The position of the rhamnose moiety was confirmed by complete methylation of the phenolic hydroxyl groups and hydrolysis to dihydro-3′ : 4′ : 5 : 7-tetra-*O*-methylquercetin.

Astilbin has previously been isolated only from the rhizomes of *Astilbe odontophylla* (var. congesta),[1] *Astilbe thunbergi*,[3] and the leaves of *Litsea glauca*.[4] Neither astilbin nor dihydroquercetin was found in the leaves of *Quintinnia serrata* when a methanolic extract was examined by paper chromatography.

Experimental.—Microanalyses are by Dr. A. D. Campbell, University of Otago, N.Z. Infrared spectra were measured for KBr discs and ultraviolet spectra were measured for EtOH solutions. Circular paper chromatography was carried out on Whatman's No. 1 paper, with the following solvent systems: (A) chloroform–ethanol–water (8 : 2 : 5; lower phase); (B) 60% aqueous acetic acid; (C) phenol saturated with water at 22° (5% aqueous ferric chloride as spray reagent).

Extraction. Aerial bark (1·2 kg.) was extracted (Soxhlet) with 85% aqueous methanol for 24 hr., and the dark red extract concentrated, *in vacuo*, to 2 l. Addition of water (1 l.) and removal of further methanol, *in vacuo*, precipitated discoloured crystals (135 g.). Repetition of the process with the addition of a suitable volume of water gave further yields (15·5 g.). After removal of wax with light petroleum and repeated extraction with ether the solid consisted of a single phenolic compound, R_F 0·17 (A), 0·85 (B), 0·66 (C). Paper chromatography of the final syrupy residue from the extract and of dihydroquercetin gave identical spots, R_F 0·74 (A), 0·77 (B), 0·69 (C).

Astilbin. The solid, crystallised repeatedly from 40% ethanol, gave astilbin monohydrate, needles, m. p. 179·5° (decomp.) (lit.,[1] m. p. 179—180°) (total yield, 150 g.), $[\alpha]_D^{25}$ +4° [*c* 1·3 in Me_2CO–H_2O (1 : 1)] (Found, for sample dried at room temperature: C, 54·0; H, 5·6. Calc. for $C_{21}H_{22}O_{11},H_2O$: C, 53·9; H, 5·2%). Found, for sample dried at 100° to constant weight: C, 56·4; H, 5·0. Calc. for $C_{21}H_{22}O_{11}$: C, 56·0; H, 4·9%). $\nu_{max.}$ 3448 (OH), 2959 (C-H), 2732 (shoulder) (C-H), 1650 (conjugated CO) cm.$^{-1}$, $\lambda_{max.}$ 292 mμ (log ε 4·21), 330 (shoulder) mμ (log ε 3·66). The heptaacetate, prepared by the use of pyridine and acetic anhydride (1 hr.; 90°), formed needles, m. p. 107°, from 50% aqueous ethanol (Found: C, 56·2, 56·0; H, 4·3, 4·7; Ac, 38·8. $C_{35}H_{36}O_{18}$ requires C, 56·4; H, 4·9; 7Ac, 40·4%), $\nu_{max.}$ 2976 (C-H), 1776 (acetate), 1761 (acetate), 1684 (conjugated CO) cm.$^{-1}$. The ferric reaction was negative and the compound was insoluble in dilute alkali.

[1] Hayashi and Ouchi, *Misc. Reports Res. Inst. Nat. Resources, Japan*, 1950, No. 17—18, 19; *Chem. Abs.*, 1953, **47**, 705.
[2] *Idem, ibid.*, 1953, No. 32, 1; *Chem. Abs.*, 1954, **48**, 13841.
[3] Shimada, Sawada, and Fukuda, *J. Pharm. Soc. Japan*, 1952, **72**, 578; *Chem. Abs.*, 1952, **46**, 8810.
[4] Nakabayashi, *J. Agr. Chem. Soc. Japan*, 1952, **26**, 469; *Chem. Abs.*, 1954, **48**, 5942.

Methylation of astilbin in methanol–ether (1 : 1) with diazomethane at 0°, or with dimethyl sulphate and anhydrous potassium carbonate in dry acetone for 60 hr., gave the tetramethyl ether, needles (from aqueous dimethylformamide–methanol), m. p. 225—227° (lit.,[3] m. p. 226—227°) (Found: C, 57·8; H, 6·0; OMe, 23·7. Calc. for $C_{25}H_{30}O_{11},H_2O$: C, 57·2; H, 6·15; 4OMe, 23·7%), $\nu_{max.}$ 3509 (OMe), 3333 (OH), 2941 (C-H), 1672 (conjugated CO) cm.$^{-1}$. Hydrolysis with 2N-hydrochloric acid for 1 hr. and extraction with ether gave dihydro-3′ : 4′ : 5 : 7-tetra-*O*-methylquercetin (needles from 90% ethanol), m. p. and mixed m. p. 168—169°.

Hydrolysis of astilbin. Astilbin monohydrate (6·52 g.), hydrolysed with 7% sulphuric acid (150 c.c.) for 2 hr., yielded the aglycone (4·03 g.) (Found: aglycone, 64·5. $C_{21}H_{22}O_{10},H_2O$ requires aglycone, 64·9%). Repeated crystallisation from hot water (charcoal) gave optically inactive, hexagonal rods, m. p. and mixed m. p. 239—240° (decomp.) with (±)-dihydroquercetin, prepared by racemisation of authentic (+)-dihydroquercetin, $[\alpha]_D^{25}$ +48° [*c* 1·0 in Me_2CO–H_2O (1 : 1)], by Pew's method [5] (Found: C, 59·5; H, 4·0. Calc. for $C_{15}H_{12}O_7$: C, 59·2; H, 4·0%), $\nu_{max.}$ 3410 (OH), 3289 (OH), 3195 (sh) (OH), 2959 (C-H), 1640 (conjugated CO) cm.$^{-1}$, $\lambda_{max.}$ 292 mμ (log ε 4·35), 330 (sh) mμ (log ε 3·72) [penta-acetate (needles from methanol), m. p. 152—153° (lit.,[6] m. p. 150—152°) (Found: C, 58·7; H, 4·3; Ac, 41·3. Calc. for $C_{25}H_{22}O_{12}$: C, 58·4; H, 4·3; 5Ac, 41·8%), $\nu_{max.}$ 1777 (acetate), 1740 (sh) (acetate), 1705 (conjugated CO), cm.$^{-1}$, $\lambda_{max.}$ 264 mμ (log ε 4·12), 313 mμ (log ε 3·61); tetrabenzoate (needles from ethanol), m. p. 188—189° (lit.,[7] m. p. 192°) (Found: C, 71·9; H, 4·2. Calc. for $C_{43}H_{28}O_{11}$: C, 71·6; H, 3·9%)]. The tetramethyl ether, prepared by the method of Hergert *et al.*,[8] formed granular crystals m. p. 169°, from ethyl acetate–ligroin (lit.,[8] m. p. 169—170°) [monoacetate (needles from methanol), m. p. 171—172° (lit.,[8] m. p. 171—172°)].

Comparative paper chromatography of the neutralised and concentrated hydrolysate and of rhamnose gave identical spots. The rhamnose was isolated as the *p*-nitrophenylhydrazone, m. p. and mixed m. p. 187—188°.

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University of Auckland, New Zealand. [*Received, August 18th*, 1958.]

[5] Pew, *J. Amer. Chem. Soc.*, 1948, **70**, 3031.
[6] Nishida, Ito, and Kondo, *J. Japan Tech. Assoc. Pulp Paper Ind.*, 1952, **6**, 261, 332; *Chem. Abs.*, 1952, **46**, 11343.
[7] Kondo, *J. Fac. Agr. Kyushi Univ., Japan*, 1951, **10**, 79; *Chem. Abs.*, 1953, **47**, 4602.
[8] Hergert, Coad, and Logan, *J. Org. Chem.*, 1956, **21**, 304.

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172. *Molecular-orbital Treatment of Compounds containing Intramolecular Hydrogen Bonds.*

By S. Marcinkiewicz and J. Green.

Hunsberger *et al.*,[1] studying the infrared spectra of a number of aromatic compounds containing vicinal hydroxy- and carbonyl groups, found that the strength of the intramolecular hydrogen-bond varies with the amount of double-bond character exhibited by the ring bond between the carbon atoms bearing the chelated substituents. A linear relation was observed between Δν(C=O) and Pauling's percentage double-bond character for the ring bonds in benzene, naphthalene, and phenanthrene. The linear relation was not perfect, since Δν(C=O) values for the isomeric 1 : 2- and 2 : 1-derivatives of naphthalene were appreciably different. Also the linearity did not extend to aliphatic compounds, since the double bond in propene was found to correspond to approximately the same Δν(C=O) value as the 9 : 10-bond in phenanthrene. To account for these phenomena, Hunsberger *et al.*[1d] postulated a novel concept of steric facilitation of chelation.

The study of the chelated hydrogen bond may become a valuable method in the study

[1] (*a*) Hunsberger, *J. Amer. Chem. Soc.*, 1950, **72**, 5626; (*b*) Hunsberger, Ketcham, and Gutowsky, *ibid.*, 1952, **74**, 4839; (*c*) Hunsberger, Lednicer, Gutowsky, Bunker, and Taussig, *ibid.*, 1955, **77**, 2466; (*d*) Hunsberger, Gutowsky, Powell, Morin, and Bandurco, *ibid.*, 1958, **80**, 3294.

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of aromatic character and related problems and, therefore, it was of interest to consider the data reported by Hunsberger *et al.* from the point of view of the molecular-orbital theory.[2]

It may be assumed that the strength of the intramolecular hydrogen bond in *o*-hydroxy-ketones, -aldehydes, and -esters depends not only on the bond order of the bonds between the carbon atoms bearing the chelated substituents, but also on the tendency of the carbonyl-oxygen atom to form a hydrogen bond, and hence on the free valence of the ring-carbon atom bearing the carbonyl group.[3] If it is further assumed that $\Delta\nu$(C=O) is a linear function of bond order and free valence in the parent hydrocarbon, the general expression correlating $\Delta\nu$(C=O) with the wave-mechanical quantities will be:

$$\Delta\nu(\text{C=O}) = K \cdot p_{rs} + L(N_{\max.} - \sum_s p_{rs}) + M \quad . \quad . \quad . \quad . \quad (1)$$

where p_{rs} stands for the mobile bond order of the bond bearing the chelated substituents and s in summation applies to all ring-carbon atoms adjacent to the carbon atom r that bears the carbonyl group. $N_{\max.}$ is the highest value the bond number may take, and is equal to $\sqrt{3}$ for tertiary, $\sqrt{2}$ for secondary, and 1 for primary carbon atoms, all in conjugated systems.[4] K, L, M are parameters characteristic for the type of the carbonyl group forming the chelated hydrogen bond with the hydroxyl group.

Substituting the values of $\Delta\nu$(C=O), representing the average values of $\Delta\nu$(C=O) of esters, ketones, and aldehydes reported by Hunsberger *et al.* for the aromatic compounds studied by them, we obtain a set of five equations:

$$43\ (\pm 1) = 0{\cdot}667K + 0{\cdot}080L + M \text{ (for 1-hydroxy-2-Y*-benzene)}$$
$$59\ (\pm 1) = 0{\cdot}725K + 0{\cdot}134L + M \text{ (for 2-hydroxy-1-Y*-naphthalene)}$$
$$54\ (\pm 1) = 0{\cdot}725K + 0{\cdot}086L + M \text{ (for 1-hydroxy-2-Y*-naphthalene)}$$
$$29\ (\pm 1) = 0{\cdot}603K + 0{\cdot}086L + M \text{ (for 2-hydroxy-3-Y*-naphthalene)}$$
$$70\ (\pm 1) = 0{\cdot}775K + 0{\cdot}133L + M \text{ (for 9-hydroxy-10-Y*-phenanthrene)}$$

Y* = Carbonyl substituent.

The equations are consistent for values of K, L, and M of 205, 104, and −103, respectively. While the data from the experiments of Hunsberger *et al.* are scanty, it is unlikely that the agreement is fortuitous, and it appears that the infrared spectra of the chelated compounds can be interpreted without postulating other than electronic effects. Equation (1) explains also the apparently anomalous value of $\Delta\nu$(C=O) for methyl acetoacetate (Hunsberger *et al.*). The free valence at the end of the double bond in propene distant from the methyl group is $1 - p_{rs}$. Substituting this in equation (1) and solving it leads to the values for the bond order and free valence at the end of the double bond in propene as 0·85 and 0·15, respectively. These figures, which are of the right order, reflect delocalisation of π-electrons in propene owing to hyperconjugation.

In two recent papers, Hunsberger *et al.*[1c,d] have applied the concept of steric facilitation of chelation to the study of the Mills–Nixon effect in tetrahydronaphthalene and indane derivatives. The available results are insufficient for the application of equation (1) to this problem, since results for at least 3 isomers in each case are required, but the results of Hunsberger *et al.* suggest greater effects of saturated rings or vicinal methyl groups on the bond orders than was calculated by Berthier and Pullman.[5]

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[*Received, October 3rd*, 1958.]

[2] Coulson, "Valence," Oxford, 1954.
[3] Pullman and Pullman, "Progress in Organic Chemistry," Butterworths, London, 1958, Vol. IV, p. 31.
[4] Moffit, footnote to Coulson, *J. Chim. phys.*, 1948, **45**, 243.
[5] Berthier and Pullman, *Bull. Soc. chim. France*, 1950, **17**, 88.

173. *Pyrrolidine- and 1-Methylpyrrolidine-3-carboxylic Acid.*

By J. F. Cavalla.

In other work it was necessary to prepare esters of the hitherto unknown pyrrolidine- and 1-methylpyrrolidine-3-carboxylic acid. Miyamoto's recent work [1] on the synthesis of pyrrolidine-3-carboxylic acid prompts us to publish our results before the completion of the main work.

For the synthesis of ethyl 1-methylpyrrolidine-3-carboxylate the method described by Bergel and his co-workers [2] for the preparation of the analogous ethyl 1-methyl-3-phenylpyrrolidine-3-carboxylate proved satisfactory. This involved catalytic reduction of ethyl γ-benzylmethylamino-α-cyanobutyrate with palladised charcoal, both the cyano- and the benzylmethylamino-group being reduced and the molecule cyclised with elimination of toluene and ammonia.

Many methods were tried before a satisfactory synthesis was evolved for the unsubstituted pyrrolidine-3-carboxylic acid. Bergel *et al.*[2] prepared 3-phenylpyrrolidine-3-carboxylic acid in small yield by catalytic reduction of ethyl αβ-dicyano-α-phenylpropionate; reduction of the simpler ethyl αβ-dicyanopropionate in our hands, however, did not give the required product. Bergel, Morrison, and Rinderknecht later reported [3] the preparation of ethyl 3-phenylpiperidine-3-carboxylate by catalytic reduction of ethyl 5-dibenzylamino-2-cyano-3-phenylpentanoate. Reduction of ethyl γ-dibenzylamino-α-cyanobutyrate gave the required compound on one occasion in low yield, but the experiment could not be repeated. Other methods were tried, depending on the reduction of γ-substituted α-cyanobutyric esters, amongst them the γγ-diethoxy-, the γ-hydroxy- (as the γ-lactone), the γ-benzyloxy-, the γ-ethoxy- and the γ-diethylamino-ester, but in each case reduction of the cyano-group proved unsatisfactory, ammonia being formed. The final satisfactory method started from ethane-1 : 1 : 2-tricarboxylic acid. A Mannich-type reaction with this acid, benzylamine, and formaldehyde gave α-benzylaminomethylsuccinic acid which, on esterification and distillation, gave its lactam, ethyl 1-benzylpyrrolid-5-one-3-carboxylate. Reduction by lithium aluminium hydride gave 1-benzyl-3-hydroxymethylpyrrolidine which was oxidised to the corresponding acid and debenzylated to the required pyrrolidine-3-carboxylic acid.

Experimental.—Ethyl γ-benzylmethylamino-α-cyanobutyrate. The sodio-derivative of ethyl cyanoacetate (prepared from 26·6 g. of the ester) in absolute ethanol (50 ml.) was treated slowly at room temperature with a solution of *N*-benzyl-2-chloro-*N*-methylethylamine [4] (48·8 g.) in toluene (100 ml.). The mixture was stirred for 30 min., then refluxed with stirring for 1½ hr., cooled, filtered, and concentrated. Isolation with ether and distillation *in vacuo* gave the *product* (20·7 g.), b. p. 154°/0·6 mm., n_D^{20} 1·5026 (Found: C, 69·4; H, 7·7; N, 10·6. $C_{15}H_{20}O_2N_2$ requires C, 69·2; H, 7·7; N, 10·8%). This compound was prepared in the crude state by Schmutz and Kunzle [5] who reported that it decomposed on distillation.

Ethyl 1-methylpyrrolidine-3-carboxylate. The preceding ester (19·5 g.) in ethanol (150 ml.) was treated with 6·7N-hydrochloric acid (22·4 ml., 2 equiv.) and hydrogenated with 10% palladised charcoal (3·5 g.), the theoretical volume of hydrogen being absorbed in 4 hr. After removal of the solvent and treatment with 2N-sodium carbonate the base was isolated with ether and distilled *in vacuo*, to give the *pyrrolidine* (2·84 g.), b. p. 99°/25 mm., n_D^{20} 1·4454 (Found: C, 61·4; H, 9·4; N, 9·0. $C_8H_{15}O_2N$ requires C, 61·1; H, 9·6; N, 8·9%).

Ethyl γ-dibenzylamino-α-cyanobutyrate. Ethyl sodiocyanoacetate (34 g., 1·5 mol.) in ethyl cyanoacetate (100 ml.) was stirred at 100° with 2-dibenzylaminoethyl chloride [6] (43·5 g.) in toluene (40 ml.) for 1½ hr., then left overnight at room temperature. Water (300 ml.) was added

[1] Miyamoto, *Yakugaku Zasshi*, 1957, **77**, 568; *Chem. Abs.*, 1957, **51**, 16,422.
[2] Bergel, Hindley, Morrison, and Rinderknecht, *J.*, 1944, 269.
[3] Bergel, Morrison, and Rinderknecht, U.S.P. 2,446,804; *Chem. Abs.*, 1949, **43**, 695.
[4] Wilson, *J.*, 1952, 3524.
[5] Schmutz and Kunzle, *Helv. Chim. Acta*, 1955, **38**, 925.
[6] U.S.P., 1,949,247; *Chem. Abs.*, 1934, **28**, 2850.

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and the mixture extracted with benzene (3 × 75 ml.), and the bulked organic layers were dried (Na_2SO_4) and concentrated to a red oil. (An aliquot part of this decomposed on distillation in a high vacuum.) The oil was suspended in 6N-hydrochloric acid (250 ml.), and the insoluble portion extracted with ether and benzene; basification and isolation with benzene then gave the crude product as a cherry-red oil (17·5 g.).

Ethyl pyrrolidine-3-carboxylate. The preceding oil (13·1 g.) in ethanol (120 ml.) containing 6N-hydrobromic acid (13·1 ml., 2 equiv.) was hydrogenated with 10% palladised charcoal (2 g.) at atmospheric pressure. Absorption of hydrogen was rapid at first but became slow. Isolation as for the methyl analogue gave ethyl pyrrolidine-3-carboxylate (1·05 g.), b. p. 99—100°/14 mm., n_D^{20} 1·4568 (Found: C, 59·1; H, 8·8; N, 9·5. $C_7H_{13}O_2N$ requires C, 58·7; H, 9·2; N, 9·8%). Repetition of this reduction failed.

α-Benzylaminomethylsuccinic acid. Ethane-1 : 1 : 2-tricarboxylic acid (95 g.) in water (180 ml.) was treated with benzylamine (62 g.), then, at −2°, with aqueous 40% formaldehyde (49 ml.) and left at 0° for 3 days. The solution, containing a slimy solid, was treated with acetone and scratched, to give a white powder (120 g.), m. p. 76—115° (decomp.). This was heated in water (125 ml.) at 95° for 20 min., then cooled, and acetone was added to give the *product* (65 g.) as needles, m. p. 141—142° (Found: C, 60·7; H, 6·4; N, 5·7. $C_{12}H_{15}O_4N$ requires C, 60·8; H, 6·4; N, 5·9%).

Ethyl 1-benzyl-5-pyrrolidone-3-carboxylate. The foregoing acid (65 g.) in absolute ethanol (500 ml.) was treated with dry hydrogen chloride (40 g.) and the mixture refluxed for 8 hr. Isolation with ether and dilute potassium carbonate gave the amino-ester which lactamised on distillation *in vacuo* to give the *pyrrolidone* (56·9 g.), b. p. 175°/1·0 mm., n_D^{20} 1·5278 (Found: C, 68·6; H, 6·9; N, 5·5. $C_{14}H_{17}O_3N$ requires C, 68·0; H, 6·9; N, 5·7%).

1-Benzyl-3-hydroxymethylpyrrolidine. The pyrrolidone (56·8 g.) in dry ether (300 ml.) was added dropwise with stirring to a cooled suspension of lithium aluminium hydride (30 g.) in dry ether (500 ml.), and the mixture refluxed with stirring for 16 hr. The solution was cooled strongly, treated cautiously with water (50 ml.), and filtered, and the solid was washed with ether. The ethereal solution was concentrated to an oil and distilled *in vacuo*, to give the *alcohol* (40·6 g.), b. p. 129°/0·9 mm., n_D^{20} 1·5414 (Found: C, 75·2; H, 8·8; N, 7·3. $C_{12}H_{17}ON$ requires C, 75·4; H, 9·0; N, 7·3%). Its *oxalate* formed needles, m. p. 99—100°, from methanol–ether (Found: C, 60·2; H, 7·3; N, 5·0. $C_{12}H_{17}ON,C_2H_2O_4$ requires C, 59·8; H, 6·8; N, 5·0%).

1-Benzylpyrrolidine-3-carboxylic acid. 1-Benzyl-3-hydroxymethylpyrrolidine (25·85 g.) in 2N-sulphuric acid (150 ml.) was added dropwise with stirring to a solution of chromium trioxide (30 g.) in 2N-sulphuric acid (200 ml.) and left at room temperature overnight. The resulting dark brown solution was treated with a solution of barium hydroxide octahydrate (205 g.) in warm water (500 ml.) and filtered, and the solid washed with water. The combined filtrate and washings were extracted with ether (200 ml.), then treated with a stream of carbon dioxide, filtered, and concentrated *in vacuo*. Addition of acetone then gave the *acid* (13·9 g.), m. p. 105—107°, which crystallised from methanol–acetone as hygroscopic rods, m. p. 106—108° (Found: C, 70·0; H, 7·6; N, 6·4. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·4; N, 6·8%).

Pyrrolidine-3-carboxylic acid. The preceding acid (1·05 g.) in ethanol (100 ml.) was hydrogenated with 10% palladised charcoal (0·25 g.) at atmospheric pressure and the solution was filtered and concentrated to a mixture of crystals and oil. Crystallisation from methanol–acetone gave the *amino-acid* (0·45 g.) as hygroscopic needles, m. p. 183—185°, pK 3·38 and 10·72 (Found: C, 51·8; H, 8·0; N, 11·7. $C_5H_9O_2N$ requires C, 52·2; H, 7·9; N, 12·2%), ν (in Nujol) 722, 725, 790, 839, 864, 895, 912, 940, 967, 1015, 1048, 1060, 1110, 1171, 1195, 1295, 1307, 1352, 1565, 1656, 2366, 2764, and 3444 cm.$^{-1}$.

Methyl 1-benzylpyrrolidine-3-carboxylate. The acid (13·3 g.) in methanol (200 ml.) containing dry hydrogen chloride (15 g.) was refluxed for 5 hr. Removal of the solvent, basification, and isolation with ether gave the *ester* (8·7 g.), b. p. 122°/0·8 mm., n_D^{20} 1·5207 (Found: C, 71·5; H, 8·0; N, 6·3. $C_{13}H_{17}O_2N$ requires C, 71·2; H, 7·8; N, 6·4%).

Methyl pyrrolidine-3-carboxylate. The preceding ester (8·5 g.) was hydrogenated as for the corresponding acid, to give the *amino-ester* (3·8 g.), b. p. 92°/17 mm., n_D^{20} 1·4590 (Found: C, 56·4; H, 8·6; N, 10·7. $C_6H_{11}O_2N$ requires C, 55·8; H, 8·6; N, 10·9%).

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174. *Di*-O-cyclo*hexylidene*-D-*mannose*.

By R. D. Guthrie and John Honeyman.

Di-*O-cyclo*hexylidene-D-mannose has been prepared by condensation of D-mannose with *cyclo*hexanone in the presence of sulphuric acid. The *cyclo*hexylidene groups have been shown to occupy the 2 : 3-5 : 6-positions, as do the *iso*propylidene groups in the corresponding derivative from acetone. This is in agreement with work on D-glucose,[1,2] L-sorbose,[3,4] dulcitol,[3,5] and D-mannitol,[6] where *cyclo*hexanone has been found to react with the same positions as acetone. The compound was similar to the corresponding acetone derivative in not reducing Fehling's solution in spite of having a free 1-position.

Di-*O-cyclo*hexylidene-D-mannose was characterised by oxidation with alkaline potassium permanganate to potassium di-*O-cyclo*hexylidene-D-mannonate, whose lactone absorbed strongly at 1779 cm.$^{-1}$ in the infrared region (saturated γ-lactones [7,8] absorb at 1780—1760 cm.$^{-1}$). The lactone yielded the known 2-(D-*manno*pentahydroxypentyl)benzimidazole on reaction with *o*-phenylenediamine in the presence of hydrochloric acid to remove the ketal groups. This proved that the above oxidation occurred at the reducing centre of the mannose derivative.

Reaction with benzoyl chloride gave a monobenzoate, and reduction with sodium borohydride gave a new di-*O-cyclo*hexylidene-D-mannitol, further characterised as its dibenzoate.

Experimental.—The infrared spectra were determined for Nujol mulls. Light petroleum was the fraction of b. p. 60—80°. Alumina was type H, mesh 100/200, supplied by Peter Spence Ltd.

Di-O-cyclo*hexylidene*-D-*mannose*. D-Mannose (9 g.) was shaken for 16 hr. at room temperature with *cyclo*hexanone (20 ml.) containing sulphuric acid (1 ml.). The solid reaction mixture was warmed with *n*-heptane until two liquid layers were formed. The *n*-heptane phase was decanted and kept overnight at −40°. The resulting colourless needles (12·2 g.), m. p. 120—121°, after two recrystallisations from *n*-heptane, gave 2 : 3-5 : 6-*di*-O-cyclo*hexylidene*-D-*mannose* (11·2 g., 66%), m. p. 122°, $[\alpha]_D^{21}$ +13·4° (*c* 0·92 in chloroform), $[\alpha]_D^{20}$ +7·8° (*c* 1·29 in ethanol) (Found: C, 63·4; H, 8·0. $C_{18}H_{28}O_6$ requires C, 63·5; H, 8·3%). The product did not reduce Fehling's solution and absorbed at 3559 cm.$^{-1}$ in the OH stretching region of the infrared spectrum.

Benzoyl chloride (0·14 ml.) in pyridine (1 ml.) was added to a solution of this derivative (0·34 g.) in pyridine (1 ml.) at 0°. After 15 hr. at room temperature, the excess of benzoyl chloride was decomposed and the mixture poured into ice-water, to give yellow oil. Chloroform-extraction, concentration, chromatography of the extract on alumina, and elution with benzene gave white needles (0·15 g., 34%). Two recrystallisations from light petroleum yielded 2 : 3-5 : 6-*di*-O-cyclo*hexylidene*-D-*mannose* 1-*benzoate*, m. p. 138—139°, $[\alpha]_D^{20}$ +36·6° (*c* 1·12 in chloroform) (Found: C, 67·1; H, 7·6. $C_{25}H_{32}O_7$ requires C, 67·6; H, 7·2%).

Oxidation. Di-*O-cyclo*hexylidene-D-mannose was oxidised by alkaline potassium permanganate by Ohle and Behrend's method [9] to yield *potassium* 2 : 3-5 : 6-*di*-O-cyclo*hexylidene*-D-*mannonate* (60%), $[\alpha]_D^{15}$ −30·1° (*c* 1·08 in water). The product absorbed strongly at 1605 cm.$^{-1}$ (characteristic of the CO_2^- group) and gave a yellow precipitate with sodium cobaltinitrite. (The corresponding *iso*propylidene compound,[9] prepared similarly, absorbed strongly at 1613 cm.$^{-1}$.)

Ether was added to a solution of the potassium salt (0·95 g.) in water (40 ml.). The

[1] Hockett, Miller, and Scattergood, *J. Amer. Chem. Soc.*, 1949, **71**, 3072.
[2] Gluzman and Klyushink, *Zhur. obshchei Khim.*, 1955, **25**, 2118.
[3] Kazimirova, *ibid.*, 1954, **24**, 626.
[4] *Idem, ibid.*, 1955, **25**, 1601.
[5] *Idem, ibid.*, 1957, **27**, 981.
[6] Bourne, Corbett, and Erilinne, *J.*, 1950, 786.
[7] Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen & Co., London, 1954.
[8] Barker, Bourne, Prinkard, and Whiffen, *Chem. and Ind.*, 1958, 658.
[9] Ohle and Behrend, *Ber.*, 1925, **58**, 2590.

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theoretical quantity of N-sulphuric acid was added, and the mixture was shaken to dissolve the solid precipitate in the aqueous layer. The ether layer was separated, dried, and evaporated to a white solid, which, after two recrystallisations from light petroleum containing a little benzene, gave 2 : 3-5 : 6-*di*-O-cyclo*hexylidene*-D-*mannono*-*γ*-*lactone*, m. p. 108—110°, $[\alpha]_D^{22}$ +43·9° (*c* 1·51 in chloroform) (Found: C, 63·7; H, 7·8. $C_{18}H_{26}O_6$ requires C, 63·9; H, 7·7%).

The *γ*-lactone (0·27 g.) and *o*-phenylenediamine (0·1 g.) were heated in water (1 ml.) and hydrochloric acid (0·2 ml.) for 7 hr. in a steam-bath. After water (4 ml.) had been added, the dark solution was filtered through charcoal and neutralised with aqueous ammonia. Recrystallisation of the precipitated white solid from 30% aqueous ethanol gave 2-(D-*manno*pentahydroxypentyl)benzimidazole, m. p. 219—221° (decomp.), identified by comparison with an authentic sample, m. p. 220—221° (decomp.), $[\alpha]_D^{16}$ −23·2° (*c* 0·88 in N-hydrochloric acid), prepared by the same method from potassium 2 : 3-5 : 6-di-*O*-*iso*propylidene-D-mannonate. Haskins and Hudson [10] record m. p. 224° (decomp.), $[\alpha]_D^{20}$ −23·7° (*c* 5 in N-hydrochloric acid).

Reduction. Sodium borohydride (0·6 g.) was added to a stirred suspension of di-*O*-*cyclo*hexylidene-D-mannose (3·4 g.) in water (200 ml.) and methanol (100 ml.). After 3 hours' stirring, sodium borohydride (0·2 g.) was added. Stirring was continued for 16 hr. more, a trace of solid then remaining. After the filtered solution had been adjusted to pH 4 with dilute hydrochloric acid, the resulting white solid (3 g.), m. p. 115—120°, was collected, washed with water, and recrystallised three times from light petroleum–ethanol to give colourless needles of 1 : 2-4 : 5(or 2 : 3-5 : 6)-*di*-O-cyclo*hexylidene*-D-*mannitol*, m. p. 133—134°, $[\alpha]_D^{19}$ −11·7° (*c* 0·96 in chloroform) (Found: C, 63·6; H, 8·9. $C_{18}H_{30}O_6$ requires C, 63·1; H, 8·8%).

Complete hydrolysis was achieved by leaving a solution of the product (0·81 g.) in ethanol (60 ml.) and hydrochloric acid (20 ml.) for 14 hr. at room temperature. The solution was neutralised with lead carbonate, filtered, and concentrated to give D-mannitol (0·35 g., 78%), m. p. 160—167°, characterised as its hexa-acetate, m. p. 122—123°.

Benzoylation of the D-*mannitol derivative.* The reduced compound (0·5 g.) was benzoylated by the procedure outlined above to yield a white solid (0·47 g., 60%), m. p. 139—141°. One recrystallisation from light petroleum, followed by two from aqueous ethanol, gave 2 : 3-5 : 6-*di*-O-cyclo*hexylidene*-D-*mannitol* 1 : 4-*dibenzoate*, m. p. 141—142°, $[\alpha]_D^{19}$ −9·2° (*c* 1·63 in chloroform) (Found: C, 69·9; H, 6·9. $C_{32}H_{38}O_8$ requires C, 69·8; H, 6·9%).

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